

GenCore version 5.1.9
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OM protein - protein search, using sw model

Run on: September 21, 2006, 14:40:07 ; Search time 0.001 Seconds
(without alignments)
984.233 Million cell updates/sec

Title: US-10-668-178-2

Perfect score: 780

Sequence: 1 VRSSRTPSPXPAHVHVPN.....RPDYLDPAESGQVYFGIIAL 157

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 40 seqs, 6269 residues

Total number of hits satisfying chosen parameters: 40

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 500 summaries

Database : xedit-findpat.subdb.*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	773	99.1	157	1	ADH10160 Human tumour necro
2	766	98.2	157	1	ADH10160 TNF-R1 specific hu
3	765	98.1	157	1	ADH10160 TNF-R1 specific hu
4	764	97.9	157	1	ADH10160 TNF-R1 specific hu
5	762	97.7	157	1	ADH10160 TNF-R1 specific hu
6	759	97.3	157	1	ADH10160 TNF-R2 specific hu
7	758	97.2	157	1	ADH10160 TNF-R1 specific hu
8	754	96.7	157	1	ADH10160 TNF-R2 specific hu
9	752	96.4	157	1	ADH10160 TNF-R2 specific hu
10	751	96.3	157	1	ADH10160 TNF-R1 specific hu
11	751	96.3	157	1	ADH10160 TNF-R1 specific hu
12	751	96.3	157	1	ADH10160 TNF-R2 specific hu
13	750	96.2	157	1	ADH10160 TNF-R2 specific hu
14	750	96.2	157	1	ADH10160 TNF-R2 specific hu
15	749	96.0	157	1	ADH10160 TNF-R2 specific hu
16	749	96.0	157	1	ADH10160 TNF-R2 specific hu
17	749	96.0	157	1	ADH10160 TNF-R2 specific hu
18	749	96.0	157	1	ADH10160 TNF-R2 specific hu
19	749	96.0	157	1	ADH10160 TNF-R2 specific hu
20	749	96.0	157	1	ADH10160 TNF-R2 specific hu
21	749	96.0	157	1	ADH10160 TNF-R2 specific hu
22	748	95.9	157	1	ADH10160 TNF-R2 specific hu
23	748	95.9	157	1	ADH10160 TNF-R2 specific hu
24	748	95.9	157	1	ADH10160 TNF-R2 specific hu
25	748	95.9	157	1	ADH10160 TNF-R2 specific hu
26	747	95.8	157	1	ADH10160 TNF-R1 specific hu
27	747	95.8	157	1	ADH10160 TNF-R2 specific hu
28	747	95.8	157	1	ADH10160 TNF-R2 specific hu
29	746	95.6	157	1	ADH10160 TNF-R2 specific hu
30	746	95.6	157	1	ADH10160 TNF-R2 specific hu
31	746	95.6	157	1	ADH10160 TNF-R2 specific hu
32	746	95.6	157	1	ADH10160 TNF-R2 specific hu
33	744	95.4	157	1	ADH10160 TNF-R1 specific hu

34 743 95.3 157 1 AEB45428 TNF-R1 specific hu
35 743 95.3 157 1 AEB45425 TNF-R1 specific hu
36 742 95.1 157 1 AEB45421 Human TNF-alpha mu
37 741 95.0 157 1 AEB45427 TNF-R1 specific hu
38 741 95.0 157 1 AEB45423 Human TNF-alpha mu
39 741 95.0 157 1 AEB45435 TNF-R1 specific hu
40 698 89.5 146 1 AEB45426 TNF-R1 specific hu

ALIGNMENTS

RESULT 1

ID ADH10160 standard; protein; 157 AA.

XX AC ADH10160;

XX DT 11-MAR-2004 (first entry)

XX DE Human tumour necrosis factor variant protein.

XX KW TNF; tumour necrosis factor; polyethylene glycol; cytostatic; cancer;
human; variant.

XX OS Homo sapiens.

XX PN EPI354893-A2.

XX PD 22-OCT-2003.

XX PF 30-JAN-2003; 2003EP-00250587.

XX PR 25-MAR-2002; 2002JP-00083509.

XX PR 26-JUN-2002; 2002JP-00185387.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.

XX (MAYU/) MAYUMI T.

XX (TSUT/) TSUTSUMI Y.

XX (NAKA/) NAKAGAWA S.

XX Mayumi T, Tsutsumi Y, Nakagawa S, Ikegami H;

XX WPI; 2004-063952/07.

XX N-PSDB; ADH10169.

XX A physiologically active complex which comprises a protein part with
tumour necrosis factor activity and a high molecular part has higher
stability and retention in living bodies and is useful to treat disease,
particularly cancer.

XX Example 1; SEQ ID NO 3; 18pp; English.

XX The present sequence represents a physiologically active complex which
comprises a proteinaceous part with tumour necrosis factor (TNF) activity
and a high molecular part bound artificially to the N-terminus of the
proteinaceous part. The proteinaceous part comprises the sequence
selected from ADH10159 and the molecular part has a molecular weight of
500-5000 Da and is a homopolymer of polyethylene glycol or a copolymer of
ethylene glycol and its derivatives. The invention is used to treat
susceptible disease, particularly cancer. The complex has a higher
stability and longer retention time in living bodies than intact tumour
necrosis factor. The present sequence represents a human TNF variant
protein.

XX SQ Sequence 157 AA;

Query Match 99.1%; Score 773; DB 1; Length 157;

Best Local Similarity 96.2%; Pred. No. 0;

Matches 151; Conservative 0; Mismatches 6; Indels 0; Gaps 0;

QY 1 VRSSRTPSPXPAHVHVPNPAEQLOLNNRANALLANGVELRDNLQVWSEGLYLIYS 60
|||||

```

Db      1 VRSSRTSPDMPVHVHVANPQAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Qy      61 QVLFXGGGCPSTHVLTHITISRIASVQTVNLLSAIXSPQRETPEGAXPMYEPYIL 120
      |||||
Db      61 QVLFSGGGCPSTHVLTHITISRIASVQTVNLLSAIRSPQRETPEGANPMYEPYIL 120
Qy      121 GGVFQLEXGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
      |||||
Db      121 GGVFQLEPGDRLSAEINRPDYLDPAESGQVYFGIIAL 157

RESULT 2
ID      AEB45433
AC      AEB45433
DT      22-SEP-2005 (first entry)
DE      TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:17.
KW      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW      antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mutein.
OS      Homo sapiens.
OS      Synthetic.
PN      WO2005066206-A1.
PD      21-JUL-2005.
PX      05-JAN-2005; 2005WO-JP0000032.
PX      06-JAN-2004; 2004JP-00001427.
PA      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA      (MAYU)/ MAYUMI T.
PA      (TSUT)/ TSUTSUMI Y.
PA      (NAKA)/ NAKAGAWA S.
PI      Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
PI      WPI; 2005-506850/51.
DR      N-PSDB; AEB45447.
XX      Novel tumor necrosis factor TNF mutant protein, useful for treating
XX      and/or preventing diseases such as inflammation, and other diseases
XX      caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX      rheumatoid arthritis, allergy.
XX      Claim 4; SEQ ID NO 17; 34pp; Japanese.
XX
CC      The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC      particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC      TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC      a TNF mutant protein comprising an amino acid sequence derived from the
CC      human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC      one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC      N-terminus, and amino acid residues at positions 84-89 by other amino
CC      acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC      mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC      protein. The TNF mutant proteins are useful for treating and/or
CC      preventing diseases such as inflammation, and other diseases caused by
CC      overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC      cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC      Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,

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CC      transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC      respiratory syndrome (SARS), atherosclerosis, Bence's disease, systemic
CC      lupus erythematosus, malaria, meningitis, hepatitis, Alzheimers disease,
CC      etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC      represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC      The sequence data for this patent did not form part of the printed
CC      specification, but was obtained in electronic format directly from WIPO
CC      at ftp.wipo.int/pub/published_pct_sequences.
SQ      . Sequence 157 AA;

Query Match      98.2%; Score 766; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy      1 VRSSRTSPDXPVHVHVANPQAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
      |||||
Db      1 VRSSRTSPDMPVHVHVANPQAEQQLWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
Qy      61 QVLFXGGGCPSTHVLTHITISRIASVQTVNLLSAIXSPQRETPEGAXPMYEPYIL 120
      |||||
Db      61 QVLFSGGGCPSTHVLTHITISRIASVQTVNLLSAIRSPQRETPEGANPMYEPYIL 120
Qy      121 GGVFQLEXGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
      |||||
Db      121 GGVFQLEPGDRLSAEINRPDYLDPADGGQVYFGIIAL 157

RESULT 3
AEB45432
ID      AEB45432 standard; protein; 157 AA.
XX      AC      AEB45432;
XX      DT      22-SEP-2005 (first entry)
XX      DE      TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:16.
XX      KW      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX      KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX      KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX      KW      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX      KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX      KW      antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX      KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
XX      KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX      KW      mutein.
XX      OS      Homo sapiens.
XX      OS      Synthetic.
XX      PN      WO2005066206-A1.
XX      PD      21-JUL-2005.
XX      PX      05-JAN-2005; 2005WO-JP0000032.
XX      PX      06-JAN-2004; 2004JP-00001427.
XX      PA      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX      PA      (MAYU)/ MAYUMI T.
XX      PA      (TSUT)/ TSUTSUMI Y.
XX      PA      (NAKA)/ NAKAGAWA S.
XX      PI      Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX      PI      WPI; 2005-506850/51.
XX      DR      N-PSDB; AEB45446.
XX      Novel tumor necrosis factor TNF mutant protein, useful for treating
XX      and/or preventing diseases such as inflammation, and other diseases
XX      caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX      rheumatoid arthritis, allergy.

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XX PS Claim 4; SEQ ID NO 16; 34pp; Japanese.

XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,

XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or

XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses

XX CC a TNF mutant protein comprising an amino acid sequence derived from the

XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of

XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the

XX CC N-terminus, and amino acid residues at positions 84-89 by other amino

XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF

XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant

XX CC protein. The TNF mutant proteins are useful for treating and/or

XX CC preventing diseases such as inflammation, and other diseases caused by

XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon

XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),

XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,

XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute

XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic

XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,

XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence

XX CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:

XX CC The sequence data for this patent did not form part of the printed

XX CC specification, but was obtained in electronic format directly from WIPO

XX CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 98.1%; Score 765; DB 1; Length 157;

Best Local Similarity 94.9%; Pred. No. 0;

Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPAHVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Db 1 VRSSRTPSDMPVAVVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGGCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPQRTPEGAEXPWYPIYL 120

Db 61 QVLFPGGCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPQRTPEGAEXPWYPIYL 120

Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIAL 157

Db 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIAL 157

RESULT 4

AE45434

ID AEB45434 standard; protein; 157 AA.

XX AC AEB45434;

XX DT 22-SEP-2005 (first entry)

XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:16.

XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;

XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;

XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;

XX KW plasmoid infection; meningitis; hepatitis; Alzheimer's disease;

XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;

XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;

XX KW vasotrophic; cerebroprotective; dermatological; immunomodulator;

XX KW animalarial; antibacterial; hepatotropic; neuroprotective; nootropic;

XX KW munein.

XX OS Homo sapiens.

XX OS Synthetic.

XX XX WO200506206-A1.

XX PN 21-JUL-2005.

XX PD 05-JAN-2005; 2005WO-JP000032.

XX PF

XX PR 06-JAN-2004; 2004JP-00001427.

XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.

XX PA (MAYU/) MAYUMI T.

XX PA (TSUT/) TSUTSUMI Y.

XX PA (NAKA/) NAKAGAWA S.

XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;

XX DR WPI: 2005-506850/51.

XX DR N-PSDB; AEB45448.

XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating

XX PT and/or preventing diseases such as inflammation, and other diseases

XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,

XX PT rheumatoid arthritis, allergy.

XX PS Claim 4; SEQ ID NO 18; 34pp; Japanese.

XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,

XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or

XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses

XX CC a TNF mutant protein comprising an amino acid sequence derived from the

XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of

XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the

XX CC N-terminus, and amino acid residues at positions 84-89 by other amino

XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF

XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant

XX CC protein. The TNF mutant proteins are useful for treating and/or

XX CC preventing diseases such as inflammation, and other diseases caused by

XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon

XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),

XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,

XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute

XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic

XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,

XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence

XX CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:

XX CC The sequence data for this patent did not form part of the printed

XX CC specification, but was obtained in electronic format directly from WIPO

XX CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 97.9%; Score 764; DB 1; Length 157;

Best Local Similarity 94.9%; Pred. No. 0;

Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPAHVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Db 1 VRSSRTPSDMPVAVVAVNPAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGGCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPQRTPEGAEXPWYPIYL 120

Db 61 QVLFPGGCGPSTHLLTHTISRIAVSYQTQVNLISAIKSPQRTPEGAEXPWYPIYL 120

Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIAL 157

Db 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIAL 157

RESULT 5

AE45430

ID AEB45430 standard; protein; 157 AA.

XX AC AEB45430;

XX DT 22-SEP-2005 (first entry)

XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:14..

XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;

XX KW

KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
OS
XX
XX AC AEB45453;
PN WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
PI
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45444.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 14; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimers disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
SQ

Query Match 97.7%; Score 762; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 2; Mismatches 7; Indels 0; Gaps 0;
QY 1 VRSSRTPSDXPVAVHVNPAQEQQLWLNRRNALLANGVELNDQLVVPSEGLYLIIYS 60
DB 1 VRSSRTPSDMPVAVHVNPAQEQQLWLNRRNALLANGVELNDQLVVPSEGLYLIIYS 60
QY 61 QVLFXGGCGCSTHLLTHTTSIRIAVSQTXVNLISAIKSPQCRTPGCAEXPWYEPIYL 120
DB 61 QVLFXGGCGCSTHLLTHTTSIRIAVSQTXVNLISAIKSPQCRTPGCAEXPWYEPIYL 120

QY 121 GGVFOLEXGDRLSAEINRPDYLDRAESGOVYFGIIAL 157
DB 121 GGVFOLEPGDRLSAEINRPDYLDKDTGQVYFGIIAL 157
RESULT 6
AEB45453 ID AEB45453 standard; protein; 157 AA.
XX
XX AC AEB45453;
DT 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:37.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
OS
XX PN WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
PI
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45476.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 37; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimers disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:

CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 97.3%; Score 759; DB 1; Length 157;
 Best Local Similarity 94.9%; Pred. No. 0;
 Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDKPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFXGQGPCSTHLLTHTTISRIVSYQTQVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120
 Db 61 QVLFSGQGPCSTHLLTHTTISRIVSYQTQVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120

Qy 121 GGVFQLEKXGDRLSAEINRPNVLDPAESGQVYFGIIAL 157
 Db 121 GGVFQLEPGDRLSAEINRPNVLDPAESGQVYFGIIAL 157

RESULT 7
 AEB45431
 ID AEB45431 standard; protein; 157 AA.
 XX
 AC AEB45431;
 DT 22-SEP-2005 (first entry)
 XX

TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:15.

tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 acquired immune deficiency syndrome; severe acute respiratory syndrome;
 plasmadium infection; meningitis; hepatitis; Alzheimers disease;
 antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 vasotrophic; cerebroprotective; dermatological; immunomodulator;
 antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 mutein.

XX Homo sapiens.
 OS Synthetic.
 XX
 PN W02005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX

Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
 WPI; 2005-506850/51.
 DR N-PSDB; AEB45445.
 XX

Novel tumor necrosis factor TNF mutant protein, useful for treating
 and/or preventing diseases such as inflammation, and other diseases
 caused by overexpression of TNF, such as autoimmune diseases, tumor,
 rheumatoid arthritis, allergy.

XX
 PS Claim 4; SEQ ID NO 15; 34pp; Japanese.
 XX

The invention relates to tumor necrosis factor (TNF) mutant proteins,
 particularly tumor necrosis factor mutant proteins specific for TNF-R1 or

CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 97.2%; Score 758; DB 1; Length 157;
 Best Local Similarity 94.3%; Pred. No. 0;
 Matches 148; Conservative 0; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDKPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFXGQGPCSTHLLTHTTISRIVSYQTQVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120
 Db 61 QVLFSGQGPCSTHLLTHTTISRIVSYQTQVNLLSAIXSPCQRETPEGAEXPWYEPYIL 120

Qy 121 GGVFQLEKXGDRLSAEINRPNVLDPAESGQVYFGIIAL 157
 Db 121 GGVFQLEPGDRLSAEINRPNVLDPAESGQVYFGIIAL 157

RESULT 8
 AEB45454
 ID AEB45454 standard; protein; 157 AA.
 XX
 AC AEB45454;
 DT 22-SEP-2005 (first entry)
 XX

TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:38.

tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 acquired immune deficiency syndrome; severe acute respiratory syndrome;
 plasmadium infection; meningitis; hepatitis; Alzheimers disease;
 antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 vasotrophic; cerebroprotective; dermatological; immunomodulator;
 antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 mutein.

XX Homo sapiens.
 OS Synthetic.
 XX
 PN W02005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX

(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.

```

PA (TSUTU/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX MPI; 2005-506850/51.
XX N-PSDB; AEB45477.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 38; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 96.7%; Score 754; DB 1; Length 157;
XX Best Local Similarity 94.3%; Pred. No. 0;
XX Matches 146; Conservative 0; Mismatches 9; Indels 0; Gaps 0;
XX
Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWNTNGYANALLANGVELRDNLQVPSGLYLIYS 60
Qy 61 QVLFXGGCGCPSTHLLTHTTISRIVSVQTVNLLSIAIXSPCQRTPEGAAXPWYEPIYL 120
Db 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTVNLLSIAIXSPCQRTPEGAANPWYEPIYL 120
Qy 121 GGVFQLEXGDRLSAENRNPDLDPAESGQVYFGIALL 157
Db 121 GGVFQLEPGDRLSAENRNPDLDPAESGQVYFGIALL 157
XX
XX RESULT 9
XX AEB45469
XX ID AEB45469 standard; protein, 157 AA.
XX
XX AC AEB45469;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:53.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antiproliferic; anti-HIV; antiarteriosclerotic; immunosuppressive;

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KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
XX Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUTU/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX MPI; 2005-506850/51.
XX N-PSDB; AEB45492.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 53; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 96.4%; Score 752; DB 1; Length 157;
XX Best Local Similarity 93.6%; Pred. No. 0;
XX Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;
XX
Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
Qy 61 QVLFXGGCGCPSTHLLTHTTISRIVSVQTVNLLSIAIXSPCQRTPEGAAXPWYEPIYL 120
Db 61 QVLFSGGCGCPSTHLLTHTTISRITKYSKPVNLLSIAIXSPCQRTPEGAANPWYEPIYL 120
Qy 121 GGVFQLEXGDRLSAENRNPDLDPAESGQVYFGIALL 157
Db 121 GGVFQLEPGDRLSAENRNPDLDPAESGQVYFGIALL 157

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Sequence 157 AA;

CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 96.3%; Score 751; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFPGQGGCPSTHLLTHTTISRIVSYQTVXNLLSAIXSPCQRTPEGAXPWYEPYIL 120
 DB 61 QVLFPGQGGCPSTHLLTHTTISRIVSYQTVXNLLSAIXSPCQRTPEGAXPWYEPYIL 120
 QY 121 GGVFQLEPGDRLSABEINRPDYLDFAESGGVYFGIIL 157
 DB 121 GGVFQLEPGDRLSABEINRPDYLDFAESGGVYFGIIL 157

RESULT 12
 AEB45461
 ID AEB45461 standard; protein; 157 AA.
 XX
 AC AEB45461;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:45.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tauteumi Y, Nakagawa S, Ohta T;

DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45484.
 XX
 PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 5; SEQ ID NO 45; 34pp; Japanese.
 XX
 CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 96.3%; Score 751; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 3; Mismatches 8; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFPGQGGCPSTHLLTHTTISRIVSYQTVXNLLSAIXSPCQRTPEGAXPWYEPYIL 120
 DB 61 QVLFPGQGGCPSTHLLTHTTISRIVSYQTVXNLLSAIXSPCQRTPEGAXPWYEPYIL 120
 QY 121 GGVFQLEPGDRLSABEINRPDYLDFAESGGVYFGIIL 157
 DB 121 GGVFQLEPGDRLSABEINRPDYLDFAESGGVYFGIIL 157

RESULT 13
 AEB45460
 ID AEB45460 standard; protein; 157 AA.
 XX
 AC AEB45460;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:44.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.


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OS Synthetic.
XX WO2005066206-A1.
XX 21-JUL-2005.
XX 05-JAN-2005; 2005WO-JP000032.
XX 06-JAN-2004; 2004JP-00001427.
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU//) MAYUMI T.
XX (TSUT//) TSUTSUMI Y.
XX (NAKA//) NAKAGAWA S.
XX Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45483.
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX Claim 5; SEQ ID NO 44; 34pp; Japanese.
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-99 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX Sequence 157 AA;
XX Query Match 96.2%; Score 750; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
QY 1 VRSSSRTPSDXPVAHVANPOAEQOLWLNRRALLANGVELRDNLQVPSGGLYLYS 60
DB 1 VRSSSRTPSDMPVAHVANPOAEQOLWLNRRALLANGVELRDNLQVPSGGLYLYS 60
QY 61 QVLFKGGQCPSTHLLTHTTISRIVSYQTXVNLISAIXSPQRETPEGAEXPVVEPIYL 120
DB 61 QVLFSGGQCPSTHLLTHTTISRISVYNGPVNLLSAIRSPQRETPEGAEXPVVEPIYL 120
QY 121 GGVFQLEKGRDLRAEINRPDYLDPAESQVYFGIALL 157
DB 121 GGVFQLEPGDLRAEINRPDYLDPAESQVYFGIALL 157
RESULT 14
AEB45464
ID AEB45464 standard; protein; 157 AA.
XX

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AC AEB45464;
XX 22-SEP-2005 (first entry)
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:48.
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmoidium infection; meningitis; hepatitis; Alzheimers disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antiproliferative; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mitein.
XX Homo sapiens.
XX Synthetic.
XX WO2005066206-A1.
XX 21-JUL-2005.
XX 05-JAN-2005; 2005WO-JP000032.
XX 06-JAN-2004; 2004JP-00001427.
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU//) MAYUMI T.
XX (TSUT//) TSUTSUMI Y.
XX (NAKA//) NAKAGAWA S.
XX Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45487.
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX Claim 5; SEQ ID NO 48; 34pp; Japanese.
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-99 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX Sequence 157 AA;
XX Query Match 96.2%; Score 750; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
SQ

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QY 1 VRSSRTSPDXPVAHVANPQAEGLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
 DB 1 VRSSRTSPDXPVAHVANPQAEGLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
 QY 61 QVLFPGGCPSTHLLTHITTSRIATVSYQTXVNLISAIKSPCQRTPEGAAXPWYEPYIL 120
 DB 61 QVLFPGGCPSTHLLTHITTSRIATVSYQTXVNLISAIKSPCQRTPEGAAXPWYEPYIL 120
 QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157

RESULT 15

AEBA45472
 ID AEB45472 standard; protein; 157 AA.

XX AC AEB45472;

DT 22-SEP-2005 (first entry)

XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:56.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
 XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 XX antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 XX vasotropic; cerebroprotective; dermatological; immunomodulator;
 XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 XX mutein.

XX Homo sapiens.
 OS Synthetic.

XX WO2005066206-A1.

XX 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP000032.

XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;

XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45495.

XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.

XX Claim 5; SEQ ID NO 56; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon

CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimers disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. NO. 0;
 Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAHVANPQAEGLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60
 DB 1 VRSSRTSPDXPVAHVANPQAEGLQWLNRRNALLANGVELRDNLQVVPSEGLYLIYS 60

QY 61 QVLFPGGCPSTHLLTHITTSRIATVSYQTXVNLISAIKSPCQRTPEGAAXPWYEPYIL 120
 DB 61 QVLFPGGCPSTHLLTHITTSRIATVSYQTXVNLISAIKSPCQRTPEGAAXPWYEPYIL 120

QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIIAL 157

RESULT 16

AEBA45471
 ID AEB45471 standard; protein; 157 AA.

XX AC AEB45471;

XX 22-SEP-2005 (first entry)

XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:55.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
 XX plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 XX antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 XX vasotropic; cerebroprotective; dermatological; immunomodulator;
 XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 XX mutein.

XX Homo sapiens.
 OS Synthetic.

XX WO2005066206-A1.

XX 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP000032.

XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;

XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45494.

XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases

caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

Claim 5; SEQ ID NO 55; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R2. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.6%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVWPESEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVWPESEGLYLIYS 60
Qy 61 QVLFPGQGPCSTHLLTHTTISRIAVSYQTQVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Db 61 QVLFSGQGPCSTHLLTHTTISRIITPGVPSVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Qy 121 GGVFQLEXGDRLSAEINRDPYLDPAESGVYFGIIAL 157
Db 121 GGVFQLEPGDRLSAEINRDPYLDPAESGVYFGIIAL 157

RESULT 17
AEB45455
.ID AEB45455 standard; protein; 157 AA.

XX AEB45455;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:39.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.

OS Homo sapiens.
OS Synthetic.
XX
XX WO200506206-A1.
XX
XX 21-JUL-2005.

XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
PR
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45478.

Novel tumor necrosis factor TNF mutant protein, useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

Claim 5; SEQ ID NO 39; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R2. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.6%; Pred. No. 0;
Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVWPESEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVWPESEGLYLIYS 60
Qy 61 QVLFPGQGPCSTHLLTHTTISRIAVSYQTQVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Db 61 QVLFSGQGPCSTHLLTHTTISRIAVSYQTQVNLSSAIXSPCQRETPEGAEXPWVEPIYL 120
Qy 121 GGVFQLEXGDRLSAEINRDPYLDPAESGVYFGIIAL 157
Db 121 GGVFQLEPGDRLSAEINRDPYLDPAESGVYFGIIAL 157

RESULT 18
AEB45466
.ID AEB45466 standard; protein; 157 AA.

XX AEB45466;
XX
XX 22-SEP-2005 (first entry)
DT
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:50.

XX	XX	tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;	Db	61	QVLFGGCGPSTHVLTHITISRIKTYSHPVNLLSAIRSPCQRETPEGAENPWYEPYIL	120
KW	KW	autoimmune disease; tumor; transplant rejection; cardiovascular disease;				
KW	KW	acquired immune deficiency syndrome; severe acute respiratory syndrome;	QY	121	GGVQLEXGDRLSAENRPDYLDFASSGQVYFGIIAL	157
KW	KW	plasmodium infection; meningitis; hepatitis; Alzheimer's disease;				
KW	KW	antiinflammatory; cytostatic; antirheumatic; antithratic; antiallergic;	Db	121	GGVQLEPGDRLSAENRPDYLDFASSGQVYFGIIAL	157
KW	KW	antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;				
KW	KW	vasotropic; cerebroprotective; dermatological; immunomodulator;				
KW	KW	antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;				
XX	XX	mucin.				
XX	XX	Homo sapiens.	RESULT 19			
OS	OS	Synthetic.	ABB45474			
XX	XX	WO2005066206-A1.	ID	AEBA5474	standard; protein; 157 AA.	
PN	PN	21-JUL-2005.	XX	AEBA5474;		
PD	PD		XX	22-SEP-2005	(first entry)	
XX	XX		XX	TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:58.		
XX	XX		DE			
XX	XX		XX	tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;		
XX	XX		KW	autoimmune disease; tumor; transplant rejection; cardiovascular disease;		
XX	XX		KW	acquired immune deficiency syndrome; severe acute respiratory syndrome;		
XX	XX		KW	plasmodium infection; meningitis; hepatitis; Alzheimer's disease;		
XX	XX		KW	antiinflammatory; cytostatic; antirheumatic; antithratic; antiallergic;		
XX	XX		KW	antiporiatic; anti-HIV; antiarteriosclerotic; immunosuppressive;		
XX	XX		KW	vasotropic; cerebroprotective; dermatological; immunomodulator;		
XX	XX		KW	antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;		
XX	XX		KW	mucin.		
XX	XX		XX	Homo sapiens.		
XX	XX		OS	Synthetic.		
XX	XX		OS	WO2005066206-A1.		
XX	XX		PN	21-JUL-2005.		
XX	XX		PD			
XX	XX		XX	05-JAN-2005; 2005WO-JP000032.		
XX	XX		XX	06-JAN-2004; 2004JP-00001427.		
XX	XX		PR			
XX	XX		XX	(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.		
XX	XX		PA	(MAYU/) MAYUMI T.		
XX	XX		PA	(TSUT/) TSUTSUMI Y.		
XX	XX		PA	(NAKA/) NAKAGAWA S.		
XX	XX		PI	Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;		
XX	XX		XX	WPI; 2005-506850/51.		
XX	XX		DR	N-PSDB; AEB45497.		
XX	XX		XX	Novel tumor necrosis factor TNF mutant protein, useful for treating		
XX	XX		XX	and/or preventing diseases such as inflammation, and other diseases		
XX	XX		XX	caused by overexpression of TNF, such as autoimmune diseases, tumor,		
XX	XX		XX	rheumatoid arthritis, allergy.		
XX	XX		XX	Claim 5; SEQ ID NO 50; 34pp; Japanese.		
XX	XX		XX	The invention relates to tumor necrosis factor (TNF) mutant proteins,		
XX	XX		XX	particularly tumor necrosis factor mutant proteins specific for TNF-R1 or		
XX	XX		XX	TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses		
XX	XX		XX	a TNF mutant protein comprising an amino acid sequence derived from the		
XX	XX		XX	human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of		
XX	XX		XX	one or more amino acid residues at positions 84-89 by other amino		
XX	XX		XX	N-terminus, and amino acid residues at positions 84-89 by other amino		
XX	XX		XX	acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF		
XX	XX		XX	mutant protein; and (2) a TNF formulation comprising a TNF mutant		
XX	XX		XX	protein. The TNF mutant proteins are useful for treating and/or		
XX	XX		XX	preventing diseases such as inflammation, and other diseases caused by		
XX	XX		XX	overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon		
XX	XX		XX	cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),		
XX	XX		XX	Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,		
XX	XX		XX	transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute		
XX	XX		XX	respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic		
XX	XX		XX	lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,		
XX	XX		XX	etc. The TNF mutant proteins are highly stable in vivo. This sequence		
XX	XX		XX	represents a human TNF-alpha mutant protein specific for TNF-R2. Note:		
XX	XX		XX	The sequence data for this patent did not form part of the printed		
XX	XX		XX	specification, but was obtained in electronic format directly from WIPO		
XX	XX		XX	at ftp.wipo.int/pub/published_pct_sequences.		
XX	XX		XX	Sequence 157 AA;		
XX	XX		XX	Query Match		
XX	XX		XX	Best Local Similarity 95.0%; Score 749; DB 1; Length 157;		
XX	XX		XX	Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;		
XX	XX		XX			
XX	XX		XX	1 VRSSRTPSPXPAHVAVNPAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60		
XX	XX		XX	1 VRSSRTPSPDMPAHVAVNPAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60		
XX	XX		XX	61 QVLFGGCGPSTHVLTHITISRIASVYQTKVNLISAIKSPCQRETPEGAENPWYEPYIL 120		

CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Qy 61 QVLFXGQGCSTHLLTHITISRIASVYQTXNLLSAIXSPQRETPEGAEXPVEPIYL 120
 Db 61 QVLFXGQGCSTHLLTHITISRIASVYQTXNLLSAIXSPQRETPEGAEXPVEPIYL 120
 Qy 121 GGVFQLEPGDRLSAEINRPNPDYLDFAESGQVYFGIIAL 157
 Db 121 GGVFQLEPGDRLSAEINRPNPDYLDFAESGQVYFGIIAL 157

RESULT 20
 AEB45475
 ID AEB45475 standard; protein; 157 AA.
 XX
 AC AEB45475;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:41.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiporiatic; anti-HIV; antieriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mitein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 .FN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX
 XX 05-JAN-2005; 2005WO-JP0000032.
 XX
 PF 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45480.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 5; SEQ ID NO 41; 34pp; Japanese.
 XX

CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVNPQAEQOLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Qy 61 QVLFXGQGCSTHLLTHITISRIASVYQTXNLLSAIXSPQRETPEGAEXPVEPIYL 120
 Db 61 QVLFXGQGCSTHLLTHITISRIASVYQTXNLLSAIXSPQRETPEGAEXPVEPIYL 120
 Qy 121 GGVFQLEPGDRLSAEINRPNPDYLDFAESGQVYFGIIAL 157
 Db 121 GGVFQLEPGDRLSAEINRPNPDYLDFAESGQVYFGIIAL 157

RESULT 21
 AEB45475
 ID AEB45475 standard; protein; 157 AA.
 XX
 AC AEB45475;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:59.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiporiatic; anti-HIV; antieriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mitein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 .FN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP0000032.
 XX
 PF 06-JAN-2004; 2004JP-00001427.
 XX

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PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45498.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 59; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPKVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFXGGGCPSTHLLTHTTISRIVASYQTXXVNLLSAIXSPCQRETPGGAAXPWYEPIYL 120
Db 61 QVLFSGGCGPSTHLLTHTTISRISADYHPVNLLSAIXSPCQRETPGGAAXPWYEPIYL 120

Qy 121 GGVPQLXGGRDLAEINRDPYLDPAESGQVYFGIALL 157
Db 121 GGVPQLXGGRDLAEINRDPYLDPAESGQVYFGIALL 157

RESULT 22
ID AEB45458
AC AEB45458 standard; protein; 157 AA.
XX
XX AEB45458;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:42.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;

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KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipeoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
PD
XX
XX 05-JAN-2005; 2005WO-JP000032.
PF
XX
XX 06-JAN-2004; 2004JP-00001427.
PR
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45481.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 42; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;

Query Match 95.9%; Score 748; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPKVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVAVNPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFXGGGCPSTHLLTHTTISRIVASYQTXXVNLLSAIXSPCQRETPGGAAXPWYEPIYL 120
Db 61 QVLFSGGCGPSTHLLTHTTISRISKTYPVNLLSAIXSPCQRETPGGAAXPWYEPIYL 120

Qy 121 GGVPQLXGGRDLAEINRDPYLDPAESGQVYFGIALL 157
Db 121 GGVPQLXGGRDLAEINRDPYLDPAESGQVYFGIALL 157

```


Db	121	GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIIAL 157	
RESULT 23			
AEBA5473			
XX	ID	AEBA5473 standard; protein; 157 AA.	
XX	AC		
XX	AEBA5473;		
XX	DT	22-SEP-2005 (first entry)	
XX			
XX	DE	TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:57.	
XX	KW	tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;	
XX	KW	autoimmune disease; tumor; transplant rejection; cardiovascular disease;	
XX	KW	acquired immune deficiency syndrome; severe acute respiratory syndrome;	
XX	KW	plasmadium infection; meningitis; hepatitis; Alzheimers disease;	
XX	KW	antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;	
XX	KW	antipsoptic; anti-HIV; antiarteriosclerotic; immunosuppressive;	
XX	KW	vasotropic; cerebroprotective; dermatological; immunomodulator;	
XX	KW	antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;	
XX	XX		
XX	OS	Homo sapiens.	
XX	OS	Synthetic.	
XX	XX		
XX	XX	WO2005066206-A1.	
XX	XX		
XX	PD	21-JUL-2005.	
XX	XX		
XX	XX	05-JAN-2005; 2005WO-JP000032.	
XX	XX		
XX	XX	06-JAN-2004; 2004JP-00001427.	
XX	XX		
XX	PA	(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.	
XX	PA	(MAYU)/ MAYUMI T.	
XX	PA	(TSUT)/ TSUTSUMI Y.	
XX	PA	(NAKA)/ NAKAGAWA S.	
XX	XX		
XX	PI	Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;	
XX	XX		
XX	DR	WPI; 2005-506850/51.	
XX	DR	N-PSDB; AEB45496.	
XX	XX		
XX	XX	Novel tumor necrosis factor TNF mutant protein, useful for treating	
XX	XX	and/or preventing diseases such as inflammation, and other diseases	
XX	XX	caused by overexpression of TNF, such as autoimmune diseases, tumor,	
XX	XX	rheumatoid arthritis, allergy.	
XX	XX		
XX	PS	Claim 5; SEQ ID NO 57; 34pp; Japanese.	
XX	XX		
XX	CC	The invention relates to tumor necrosis factor (TNF) mutant proteins,	
XX	CC	particularly tumor necrosis factor mutant proteins specific for TNF-R1 or	
XX	CC	TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses	
XX	CC	a TNF mutant protein comprising an amino acid sequence derived from the	
XX	CC	human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of	
XX	CC	one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the	
XX	CC	N-terminus, and amino acid residues at positions 84-89 by other amino	
XX	CC	acid residues). Also described are: (1) a TNF inhibitor comprising a TNF	
XX	CC	mutant protein; and (2) a TNF formulation comprising a TNF mutant	
XX	CC	protein. The TNF mutant proteins are useful for treating and/or	
XX	CC	preventing diseases such as inflammation, and other diseases caused by	
XX	CC	overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon	
XX	CC	cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),	
XX	CC	Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,	
XX	CC	transplant rejection, stroke, ischemia, reestenosis, AIDS, severe acute	
XX	CC	respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic	
XX	CC	lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,	
XX	CC	etc. The TNF mutant proteins are highly stable in vivo. This sequence	
XX	CC	represents a human TNF-alpha mutant protein specific for TNF-R2. Note:	
XX	CC	The sequence data for this patent did not form part of the printed	
XX	CC	specification, but was obtained in electronic format directly from WIPO	
XX	CC	at ftp.wipo.int/pub/published_pct_sequences.	
XX	CC		
XX	SQ	Sequence 157. AA;	
XX			
XX		Query Match	95.9%; Score 748; DB 1; Length 157;
XX		Best Local Similarity	93.0%; Pred. No. 0;
XX		Matches 146; Conservative	1; Mismatches 10; Indels 0; Gaps 0;
XX	QY	1 VRSSRTPSDXPAHVAVVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60	
XX	DB	1 VRSSRTPSDMPVAHVAVVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60	
XX	QY	61 QVLFEGGCGSTHVLTHHTISRIAVSVQTXNLSAISPCORETPEGAEAXPWYEPIYL 120	
XX	DB	61 QVLFEGGCGCPSTHVLTHHTISRIATDRYSSPVNLSAISPCORETPEGAEANPWYEPIYL 120	
XX	QY	121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157	
XX	DB	121 GGVFQLEPGDRLSAEINRPDYLDFAESGQVYFGIIAL 157	
XX	RESULT 24		
XX	AEBA5467		
XX	ID	AEBA5467 standard; protein; 157 AA.	
XX	AC	AEBA5467;	
XX	XX		
XX	DT	22-SEP-2005 (first entry)	
XX	XX		
XX	DE	TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:51.	
XX	XX	tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;	
XX	KW	autoimmune disease; tumor; transplant rejection; cardiovascular disease;	
XX	KW	acquired immune deficiency syndrome; severe acute respiratory syndrome;	
XX	KW	plasmadium infection; meningitis; hepatitis; Alzheimers disease;	
XX	KW	antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;	
XX	KW	antipsoptic; anti-HIV; antiarteriosclerotic; immunosuppressive;	
XX	KW	vasotropic; cerebroprotective; dermatological; immunomodulator;	
XX	KW	antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;	
XX	XX		
XX	OS	Homo sapiens.	
XX	OS	Synthetic.	
XX	XX		
XX	XX	WO2005066206-A1.	
XX	XX		
XX	PD	21-JUL-2005.	
XX	XX		
XX	XX	05-JAN-2005; 2005WO-JP0000032.	
XX	XX		
XX	XX	06-JAN-2004; 2004JP-00001427.	
XX	XX		
XX	PA	(HAYB) HAYASHIBARA SEIBUTSU KAGAKU.	
XX	PA	(MAYU)/ MAYUMI T.	
XX	PA	(TSUT)/ TSUTSUMI Y.	
XX	PA	(NAKA)/ NAKAGAWA S.	
XX	XX		
XX	PI	Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;	
XX	XX		
XX	DR	WPI; 2005-506850/51.	
XX	DR	N-PSDB; AEB45496.	
XX	XX		
XX	XX	Novel tumor necrosis factor TNF mutant protein, useful for treating	
XX	XX	and/or preventing diseases such as inflammation, and other diseases	
XX	XX	caused by overexpression of TNF, such as autoimmune diseases, tumor,	
XX	XX	rheumatoid arthritis, allergy.	
XX	XX		
XX	PS	Claim 5; SEQ ID NO 51; 34pp; Japanese.	
XX	XX		
XX	CC	The invention relates to tumor necrosis factor (TNF) mutant proteins,	
XX	CC	particularly tumor necrosis factor mutant proteins specific for TNF-R1 or	
XX	CC	TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses	
XX	CC	a TNF mutant protein comprising an amino acid sequence derived from the	
XX	CC	human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of	
XX	CC	one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the	
XX	CC	N-terminus, and amino acid residues at positions 84-89 by other amino	
XX	CC	acid residues). Also described are: (1) a TNF inhibitor comprising a TNF	
XX	CC	mutant protein; and (2) a TNF formulation comprising a TNF mutant	
XX	CC	protein. The TNF mutant proteins are useful for treating and/or	
XX	CC	preventing diseases such as inflammation, and other diseases caused by	
XX	CC	overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon	
XX	CC	cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),	
XX	CC	Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,	
XX	CC	transplant rejection, stroke, ischemia, reestenosis, AIDS, severe acute	
XX	CC	respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic	
XX	CC	lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,	
XX	CC	etc. The TNF mutant proteins are highly stable in vivo. This sequence	
XX	CC	represents a human TNF-alpha mutant protein specific for TNF-R2. Note:	
XX	CC	The sequence data for this patent did not form part of the printed	
XX	CC	specification, but was obtained in electronic format directly from WIPO	
XX	CC	at ftp.wipo.int/pub/published_pct_sequences.	


```
XX Homo sapiens.
OS Synthetic.
XX WO2005066206-A1.
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX 06-JAN-2004; 2004JP-00001427.
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45451.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 21; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
Query Match 95.8%; Score 747; DB 1; Length 157;
Best Local Similarity 92.4%; Pred. No. 0;
Matches 145; Conservative 3; Mismatches 9; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDPVHVVANVPAEQQLWLNRRALLANGVELDQNLVWPSGLYLYS 60
Db 1 VRSSRTPSDPVHVVANVPAEQQLWLNRRALLANGVELDQNLVWPSGLYLYS 60
Qy 61 QVLFPGQCPSTHLLTTHTRISAVSYQTXYNLSAIXSPCQRTPEGAAXPWPEIYL 120
Db 61 QVLFPGQCPSTHLLTTHTRISAVSYQTXYNLSAIXSPCQRTPEGAAXPWPEIYL 120
Qy 121 GGVLQEXGDRLSAEINRPDYLDFAESGVYFGIALL 157
Db 121 GGVLQEXGDRLSAEINRPDYLDFAESGVYFGIALL 157
XX
RESULT 27
AEB45462
```

```
ID
XX AEB45462 standard; protein; 157 AA.
AC AEB45462;
XX
XX 22-SEP-2005 (first entry)
DT
XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:46.
DE
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
PD
XX
XX 05-JAN-2005; 2005WO-JP000032.
PF
XX
XX 06-JAN-2004; 2004JP-00001427.
PR
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45485.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 46; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
Query Match 95.8%; Score 747; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
```

Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAVHVVANPQAEGLQWLNRRANALLANGVELRDNLQVVPSEGLYLYS 60
 |||||
 Db 1 VRSSRTSPDXPVAVHVVANPQAEGLQWLNRRANALLANGVELRDNLQVVPSEGLYLYS 60
 |||||

QY 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||
 Db 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||

QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGGVYFGIALL 157
 |||||
 Db 121 GGVFQLEPGDRLSAEINRDPYLDFAESGGVYFGIALL 157
 |||||

RESULT 28
 AEB45470
 ID AEB45470 standard; protein; 157 AA.

XX AC AEB45470;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:54.
 XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmoidium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipeoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nontropic;
 KW mutein.
 XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO2005066206-A1.
 XX PD 21-JUL-2005.
 XX PF 05-JAN-2005; 2005WO-JP000032.
 XX PR 06-JAN-2004; 2004JP-00001427.
 XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX PA (MAYU/) MAYUMI T.
 XX PA (TSUT/) TSUTSUMI Y.
 XX PA (NAKA/) NAKAGAWA S.
 XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX DR N-PSDB; AEB45493.
 XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX PS Claim 5; SEQ ID NO 54; 34pp; Japanese.
 XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or

CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.8%; Score 747; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAVHVVANPQAEGLQWLNRRANALLANGVELRDNLQVVPSEGLYLYS 60
 |||||
 Db 1 VRSSRTSPDXPVAVHVVANPQAEGLQWLNRRANALLANGVELRDNLQVVPSEGLYLYS 60
 |||||

QY 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||
 Db 61 QVLFQXGQCPSTHLLTHTISRTAVSYQTKVNLLSAIXSPCORETPEGAEAXPWYEPYIL 120
 |||||

QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGGVYFGIALL 157
 |||||
 Db 121 GGVFQLEPGDRLSAEINRDPYLDFAESGGVYFGIALL 157
 |||||

RESULT 29
 AEB45456
 ID AEB45456 standard; protein; 157 AA.
 XX AC AEB45456;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:40.
 XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmoidium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipeoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nontropic;
 KW mutein.
 XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO2005066206-A1.
 XX PD 21-JUL-2005.
 XX PF 05-JAN-2005; 2005WO-JP000032.
 XX PR 06-JAN-2004; 2004JP-00001427.
 XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX PA (MAYU/) MAYUMI T.
 XX PA (TSUT/) TSUTSUMI Y.
 XX PA (NAKA/) NAKAGAWA S.
 XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX DR N-PSDB; AEB45479.

PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
PS Claim 5; SEQ ID NO 40; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;
Query Match 95.6%; Score 746; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVWVSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEQQLWKNAGANALLANGVELRDNLQVWVSEGLYLIYS 60
Qy 61 QVLFQGXGDRLSAEINRPDYLDAESQGVYFGIIAL 120
Db 61 QVLFSGQGCPSPTHVLLTHTISRIVSVYQTVNLLSAIRSPCQRETPEGAEXPWYEPIYL 120
Qy 121 GGVFQLEPGDRLSAEINRPDYLDAESQGVYFGIIAL 157
Db 121 GGVFQLEPGDRLSAEINRPDYLDAESQGVYFGIIAL 157
RESULT 30
AEB45459
ID AEB45459 standard; protein; 157 AA.
XX
AC AEB45459;
XX
XX 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:43.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritis; antiallergic;
KW antipapillary; anti-Hiv; antiarteriosclerotic; immunosuppressive;
KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW muten.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
PN

XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP0000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB.) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Teutsuni Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45482.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
PS Claim 5; SEQ ID NO 43; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;
Query Match 95.6%; Score 746; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVWVSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLQVWVSEGLYLIYS 60
Qy 61 QVLFQGXGDRLSAEINRPDYLDAESQGVYFGIIAL 157
Db 61 QVLFSGQGCPSPTHVLLTHTISRIVSVYQTVNLLSAIRSPCQRETPEGAEXPWYEPIYL 120
Qy 121 GGVFQLEPGDRLSAEINRPDYLDAESQGVYFGIIAL 157
Db 121 GGVFQLEPGDRLSAEINRPDYLDAESQGVYFGIIAL 157
RESULT 31
AEB45465
ID AEB45465 standard; protein; 157 AA.
XX
AC AEB45465;
XX
XX 22-SEP-2005 (first entry)
DT

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XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:49.
XX
XX
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW mutein.
XX
XX OS Homo sapiens.
XX OS Synthetic.
XX
XX PN WO2005066206-A1.
XX
XX PD 21-JUL-2005.
XX
XX PF 05-JAN-2005; 2005WO-JP000032.
XX
XX PR 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX
XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX DR N-PSDB; AEB45488.
XX
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX
XX PS Claim 5; SEQ ID NO 49; 34pp; Japanese.
XX
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins.
XX CC Particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX SQ Sequence 157 AA;
XX
XX Query Match 95.6%; Score 746; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;
XX
XX QY 1 VRSSRTPSDXPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLQVVPSEGLYLYS 60
XX , Db 1 VRSSRTPSDMPVAHVAVNPAEQQLQWLNRRANALLANGVELRDNLQVVPSEGLYLYS 60

```

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QY 61 QVLFQGGCPSTHVLTLTHTRISRIAVSYQTXVNLLSAIXSPCQRETPEGAEANPWYEPYVL 120
Db 61 QVLFQGGCPSTHVLTLTHTRISRIATHKYPQVNLLSAIXSPCQRETPEGAEANPWYEPYVL 120
QY 121 GGVFQLEEXGDRLSAEINRPDYLDFAESGGVYFGIALL 157
Db 121 GGVFQLEPDRLSAEINRPDYLDFAESGGVYFGIALL 157
RESULT 32
AEB45463
ID AEB45463 standard; protein; 157 AA.
XX
XX AC AEB45463;
XX
XX DT 22-SEP-2005 (first entry)
XX
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:47.
XX
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW mutein.
XX
XX OS Homo sapiens.
XX OS Synthetic.
XX
XX PN WO2005066206-A1.
XX
XX PD 21-JUL-2005.
XX
XX PF 05-JAN-2005; 2005WO-JP000032.
XX
XX PR 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX
XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX DR WPI; 2005-506850/51.
XX DR N-PSDB; AEB45486.
XX
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX
XX PS Claim 5; SEQ ID NO 47; 34pp; Japanese.
XX
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute

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CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPAHVAVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFKGGCGPSTHLLTHTTISRIVSYQTWNLLSAIXSPCQRTTPGAEAPWYEPIYL 120
 Db 61 QVLFSGGCGPSTHLLTHTTISRIVSYQTWNLLSAIXSPCQRTTPGAEAPWYEPIYL 120

Qy 121 GGVFQLEPGDRLSAEINRDPYLDPAESGQVYFGIIL 157
 Db 121 GGVFQLEPGDRLSAEINRDPYLDPAESGQVYFGIIL 157

RESULT 33
 AEB45429
 ID AEB45429 standard; protein; 157 AA.

XX AC AEB45429;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:13.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO2005066206-A1.
 XX PD 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP0000032.
 XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX N-PSDB; AEB45443.

XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX

PS Claim 4; SEQ ID NO 13; 34pp; Japanese.
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.4%; Score 744; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPAHVAVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFKGGCGPSTHLLTHTTISRIVSYQTWNLLSAIXSPCQRTTPGAEAPWYEPIYL 120
 Db 61 QVLFSGGCGPSTHLLTHTTISRIVSYQTWNLLSAIXSPCQRTTPGAEAPWYEPIYL 120

Qy 121 GGVFQLEPGDRLSAEINRDPYLDPAESGQVYFGIIL 157
 Db 121 GGVFQLEPGDRLSAEINRDPYLDPAESGQVYFGIIL 157

RESULT 34
 AEB45428
 ID AEB45428 standard; protein; 157 AA.

XX AC AEB45428;
 XX DT 22-SEP-2005 (first entry)
 XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:12.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX OS Homo sapiens.
 XX OS Synthetic.
 XX PN WO2005066206-A1.
 XX PD 21-JUL-2005.
 XX 05-JAN-2005; 2005WO-JP0000032.

```

PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45442.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 12; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match 95.3%; Score 743; DB 1; Length 157;
Best Local Similarity 92.4%; Pred. No. 0;
Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWRNHSNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFPGQGCPSHTVLLTHTTISRIASVQTVNLLSALXSPCQRTPGGAXPWEPIYL 120
Db 61 QVLFSGQGCPSHTVLLTHTTISRIASVQTVNLLSALXSPCQRTPGGAXPWEPIYL 120
Qy 121 GGVFQLEPGRDLSAEINRPDYLDPAESQGVYFGIALL 157
Db 121 GGVFQLEPGRDLSAEINRPDYLDPNNAQVYFGIALL 157

RESULT 35
AEB45425
ID AEB45425 standard; protein; 157 AA.
XX
XX AEB45425;
XX
XX 22-SEP-2005 (first entry)
XX
XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:9.
DE tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW

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KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; anti-allergic;
KW anti-neoplastic; anti-HIV; anti-arteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutuin.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
PD
PF 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45439.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 9; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;

Query Match 95.3%; Score 743; DB 1; Length 157;
Best Local Similarity 92.4%; Pred. No. 0;
Matches 145; Conservative 2; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWRNHSNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFPGQGCPSHTVLLTHTTISRIASVQTVNLLSALXSPCQRTPGGAXPWEPIYL 120
Db 61 QVLFSGQGCPSHTVLLTHTTISRIASVQTVNLLSALXSPCQRTPGGAXPWEPIYL 120

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Qy      121 GGVFQLEKGRDLSAEINRPDYLDFAESGQVYFGIALL 157
Db      121 GGVFQLEKGRDLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 36
AEB45421
ID      AEB45421 standard; protein; 157 AA.
XX
AC      AEB45421;
XX
DT      22-SEP-2005 (first entry)
XX
DE      Human TNF-alpha mutant protein, SEQ ID No:5.
XX
KW      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW      antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mutein.
XX
OS      Homo sapiens.
OS      Synthetic.
XX
PN      WO2005066206-A1.
XX
PD      21-JUL-2005.
XX
PF      05-JAN-2005; 2005WO-JP000032.
XX
PR      06-JAN-2004; 2004JP-00001427.
XX
PA      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA      (MAYU)/ MAYUMI T.
PA      (TSUT)/ TSUTSUMI Y.
PA      (NAKA)/ NAKAGAWA S.
XX
PI      Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
WI      WPI; 2005-506850/51.
XX
N-PSDB; AEB45422.

Novel tumor necrosis factor TNF mutant protein, useful for treating
and/or preventing diseases such as inflammation, and other diseases
caused by overexpression of TNF, such as autoimmune diseases, tumor,
rheumatoid arthritis, allergy.

Example 1; SEQ ID NO 5; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins,
particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
a TNF mutant protein comprising an amino acid sequence derived from the
human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
N-terminus, and amino acid residues at positions 84-89 by other amino
acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
mutant protein; and (2) a TNF formulation comprising a TNF mutant
protein. The TNF mutant proteins are useful for treating and/or
preventing diseases such as inflammation, and other diseases caused by
overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
etc. The TNF mutant proteins are highly stable in vivo. This sequence
represents human TNF-alpha mutant protein. Note: The sequence data for
this patent did not form part of the printed specification, but was

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```

CC      obtained in electronic format directly from WIPO at
CC      ftp.wipo.int/pub/published_pct_sequences.
XX
SQ      Sequence 157 AA;

Query Match      95.1%; Score 742; DB 1; Length 157;
Best Local Similarity 92.4%; Pred. No. 0;
Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;

Qy      1 VRSSRTSPDXPVAVHVVANPQAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db      1 VRSSRTSPDXPVAVHVVANPQAEQQLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

Qy      61 QVLFQGGQCPSTHVLTHLTISRIAVSYQTPVNLLSAIXSPCORETPGAEANPWYEPIYL 120
Db      61 QVLFQGGQCPSTHVLTHLTISRIAVSYQTPVNLLSAIXSPCORETPGAEANPWYEPIYL 120

Qy      121 GGVFQLEKGRDLSAEINRPDYLDFAESGQVYFGIALL 157
Db      121 GGVFQLEKGRDLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 37
AEB45427
ID      AEB45427 standard; protein; 157 AA.
XX
AC      AEB45427;
XX
DT      22-SEP-2005 (first entry)
XX
DE      TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:11.
XX
KW      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW      antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mutein.
XX
OS      Homo sapiens.
OS      Synthetic.
XX
PN      WO2005066206-A1.
XX
PD      21-JUL-2005.
XX
PF      05-JAN-2005; 2005WO-JP000032.
XX
PR      06-JAN-2004; 2004JP-00001427.
XX
PA      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA      (MAYU)/ MAYUMI T.
PA      (TSUT)/ TSUTSUMI Y.
PA      (NAKA)/ NAKAGAWA S.
XX
PI      Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
WI      WPI; 2005-506850/51.
XX
N-PSDB; AEB45441.

Novel tumor necrosis factor TNF mutant protein, useful for treating
and/or preventing diseases such as inflammation, and other diseases
caused by overexpression of TNF, such as autoimmune diseases, tumor,
rheumatoid arthritis, allergy.

Claim 4; SEQ ID NO 11; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins,
particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses

```

CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;
 QY 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLPXGQGCSTHLLTHTTISRIVASVQTQVNLLSAIXSPCQRETPGAXPWYEPIYL 120
 DB 61 QVLPXGQGCSTHLLTHTTISRIVASVQTQVNLLSAIXSPCQRETPGAXPWYEPIYL 120
 QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157
 DB 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157

RESULT 38
 AEB45423
 ID AEB45423 standard; protein; 157 AA.
 AC AEB45423;
 XX
 XX 22-SEP-2005 (first entry)
 DT
 DE Human TNF-alpha mutant protein, SEQ ID No:7.
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW muten.

OS Homo sapiens.
 OS Synthetic.
 XX
 XX WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEITBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.

(NAKA/) NAKAGAWA S.

Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;

WPI: 2005-506850/51.

N-PSDB; AEB45424.

Novel tumor necrosis factor TNF mutant protein, useful for treating
 and/or preventing diseases such as inflammation, and other diseases
 caused by overexpression of TNF, such as autoimmune diseases, tumor,
 rheumatoid arthritis, allergy.

Example 1; SEQ ID NO 7; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins,
 particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 a TNF mutant protein comprising an amino acid sequence derived from the
 human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 N-terminus, and amino acid residues at positions 84-89 by other amino
 acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 mutant protein; and (2) a TNF formulation comprising a TNF mutant
 protein. The TNF mutant proteins are useful for treating and/or
 preventing diseases such as inflammation, and other diseases caused by
 overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 etc. The TNF mutant proteins are highly stable in vivo. This sequence
 represents human TNF-alpha mutant protein. Note: The sequence data for
 this patent did not form part of the printed specification, but was
 obtained in electronic format directly from WIPO at
 ftp.wipo.int/pub/published_pct_sequences.

Sequence 157 AA;

Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

DB 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

QY 61 QVLPXGQGCSTHLLTHTTISRIVASVQTQVNLLSAIXSPCQRETPGAXPWYEPIYL 120

DB 61 QVLPXGQGCSTHLLTHTTISRIVASVQTQVNLLSAIXSPCQRETPGAXPWYEPIYL 120

QY 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157

DB 121 GGVFQLEPGDRLSAEINRDPYLDFAESGQVYFGIALL 157

RESULT 39

AEB45435

ID AEB45435 standard; protein; 157 AA.

AC AEB45435;

XX

XX 22-SEP-2005 (first entry)

DT

XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:19.

DE

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;

KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;

KW acquired immune deficiency syndrome; severe acute respiratory syndrome;

KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;

KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;

KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;

KW vasotropic; cerebroprotective; dermatological; immunomodulator;

```
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP0000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU) MAYUMI T.
XX (TSUT) TSUTSUMI Y.
XX (NAKA) NAKAGAWA S.
XX
XX Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45449.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 19; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 95.0%; Score 741; DB 1; Length 157;
XX Best Local Similarity 92.4%; Pred. No. 0;
XX Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;
XX
XX 1 VRSSRTSDXPFVAVHVNPAEQGLQWLNRRNALLANGVELRDNLQVLPSEGLIYLS 60
XX
XX 1 VRSSRTSDXPFVAVHVNPAEQGLQWLNRRNALLANGVELRDNLQVLPSEGLIYLS 60
XX
XX 61 QVLFVGQCPSTHLLTHTTISRIVASYQTXVNLISAIQSPQRETPGEAAXPWPEIYL 120
XX
XX 61 QVLFVGQCPSTHLLTHTTISRITPAIRNPVNLISAIQSPQRETPGEAAXPWPEIYL 120
XX
XX 121 GGVFQLEKXGDRLSAENRPDYLDFAESGVVFGIATL 157
XX
XX 121 GGVFQLEKXGDRLSAENRPDYLDFAESGVVFGIATL 157
```

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RESULT 40
AEB45426
ID AEB45426 standard; protein; 146 AA.
XX
XX AEB45426;
AC
XX 22-SEP-2005 (first entry)
XX
XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:10.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX anti-inflammatory; cytostatic; antirheumatic; antithrombotic; antiallergic;
XX antiproliferative; anti-HIV; antitumor; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.
XX
XX Homo sapiens.
OS Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP0000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU) MAYUMI T.
XX (TSUT) TSUTSUMI Y.
XX (NAKA) NAKAGAWA S.
XX
XX Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45440.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 10; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 146 AA;
```

Query Match 89.5%; Score 698; DB 1; Length 146;
Best Local Similarity 93.8%; Pred. No. 0;
Matches 136; Conservative 1; Mismatches 8; Indels 0; Gaps 0;

Qy	1	VRSSRTPSDXPVAHVVANPQAEQQLWLNRRANALLANGVELRDNQLVVPSEGLYLIYS	60
Db	1	VRSSRTPSDMPVAHVVANPQAEQQLWLNRRANALLANGVELRDNQLVVPSEGLYLIYS	60
Qy	61	QVLFXGQGCPSHTVLLTHTTISRIVSYQTXXNLISAIXPCQRETPEGAEAXPWYEPYIL	120
Db	61	QVLFSGQGCPSHTVLLTHTTISRIVSYQTPVNLLSAIRSPCQRETPEGAEANPWYEPYIL	120
Qy	121	GGVFQLEXGDRLSAEINRPDYLDFA	145
Db	121	GGVFQLEPGDRLSAEINRPDYLDPS	145

Search completed: September 21, 2006, 14:40:08
Job time : 1 secs

CC ethylene glycol and its derivatives. The invention is used to treat
 CC susceptible disease, particularly cancer. The complex has a higher
 CC stability and longer retention time in living bodies than intact
 CC necrosis factor. The present sequence represents a human TNF variant
 CC protein.
 XX
 SQ Sequence 157 AA;

Query Match 99.2%; Score 774; DB 1; Length 157;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 157; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAHVAVNPQAEQQLQMLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTSPDXPVAHVAVNPQAEQQLQMLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Qy 61 QVLPFGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPGAEAXPWYEPYIL 120
 Db 61 QVLPFGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPGAEAXPWYEPYIL 120
 Qy 121 GGVPQLEKXGDRLSAEINRPDYLDFAESGGQVYFGIIAL 157
 Db 121 GGVPQLEKXGDRLSAEINRPDYLDFAESGGQVYFGIIAL 157

RESULT 2
 ADH10160
 ID ADH10160 standard; protein; 157 AA.
 AC ADH10160;
 XX
 DT 11-MAR-2004 (first entry)
 XX
 DE Human tumour necrosis factor variant protein.
 XX
 KW TNF; tumour necrosis factor; polyethylene glycol; cytostatic; cancer;
 KW human; variant.
 XX
 OS Homo sapiens.
 XX
 PN EPI354893-A2.
 XX
 PD 22-OCT-2003.
 XX
 XX 30-JAN-2003; 2003EP-00250587.
 XX
 XX 25-MAR-2002; 2002JP-00083509.
 PR
 PR 26-JUN-2002; 2002JP-00185387.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Teuteumi Y, Nakagawa S, Ikegami H;
 XX
 XX WPI; 2004-063952/07.
 DR
 DR N-PSDB; ADH10169.
 XX
 XX A physiologically active complex which comprises a protein part with
 PT tumor necrosis factor activity and a high molecular part has higher
 PT stability and retention in living bodies and is useful to treat disease,
 PT particularly cancer.
 XX
 XX Example 1; SEQ ID NO 3; 18pp; English.
 PS
 XX The present sequence represents a physiologically active complex which
 CC comprises a proteinaceous part with tumour necrosis factor (TNF) activity
 CC and a high molecular part bound artificially to the N-terminus of the
 CC proteinaceous part. The proteinaceous part comprises the sequence
 CC selected from ADH10159 and the molecular part has a molecular weight of
 CC 500-5000 Da and is a homopolymer of polyethylene glycol or a copolymer of
 CC ethylene glycol and its derivatives. The invention is used to treat

CC susceptible disease, particularly cancer. The complex has a higher
 CC stability and longer retention time in living bodies than intact tumour
 CC necrosis factor. The present sequence represents a human TNF variant
 CC protein.
 XX
 SQ Sequence 157 AA;

Query Match 99.1%; Score 773; DB 1; Length 157;
 Best Local Similarity 96.2%; Pred. No. 0;
 Matches 151; Conservative 0; Mismatches 6; Indels 0; Gaps 0;

Qy 1 VRSSRTSPDXPVAHVAVNPQAEQQLQMLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Db 1 VRSSRTSPDXPVAHVAVNPQAEQQLQMLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 Qy 61 QVLPFGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPGAEAXPWYEPYIL 120
 Db 61 QVLPFGQGCPSHTVLLTHTTISRIVASYQTAVNLSAIXSPCQRETPGAEAXPWYEPYIL 120
 Qy 121 GGVPQLEKXGDRLSAEINRPDYLDFAESGGQVYFGIIAL 157
 Db 121 GGVPQLEKXGDRLSAEINRPDYLDFAESGGQVYFGIIAL 157

RESULT 3
 AEB45433
 ID AEB45433 standard; protein; 157 AA.
 AC AEB45433;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:17.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antinatal; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mucin.
 XX
 XX Homo sapiens.
 OS Synthetic.
 OS
 XX WO2005066206-A1.
 PN
 XX 21-JUL-2005.
 PD
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 PR
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Tsuteumi Y, Nakagawa S, Ohta T;
 XX
 XX WPI; 2005-506850/51.
 DR
 DR N-PSDB; AEB45447.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 4; SEQ ID NO 17; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC

particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R1. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

XX Sequence 157 AA;

Query Match 98.2%; Score 766; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIRSPCQRTPEGAEXPWYEPYIL 120
Db 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIRSPCQRTPEGAEXPWYEPYIL 120
Qy 121 GGVFQLEPGRDLSEINRPDYLDPFASGQVYFGIALL 157
Db 121 GGVFQLEPGRDLSEINRPDYLDPFADDDGQVYFGIALL 157

RESULT 4
AEB45432
ID AEB45432 standard; protein; 157 AA.

XX AEB45432;

XX 22-SEP-2005 (first entry)

XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:16.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.

XX Homo sapiens.

OS Synthetic.

XX WO2005066206-A1.

XX 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP000032.

XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.

(MAYU/) MAYUMI T.
(TSUT/) TSUTSUMI Y.
(NAKA/) NAKAGAWA S.

Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;

WPI; 2005-506850/51.

N-PSDB; AEB45446.

Novel tumor necrosis factor TNF mutant protein, useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

Claim 4; SEQ ID NO 16; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R1. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

XX Sequence 157 AA;

Query Match 98.1%; Score 765; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 1; Mismatches 7; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIRSPCQRTPEGAEXPWYEPYIL 120
Db 61 QVLFSGGCGCPSTHLLTHTTISRIVSVQTXVNLLSAIRSPCQRTPEGAEXPWYEPYIL 120

Qy 121 GGVFQLEPGRDLSEINRPDYLDPFASGQVYFGIALL 157
Db 121 GGVFQLEPGRDLSEINRPDYLDPFRETGQVYFGIALL 157

RESULT 5
AEB45434

ID AEB45434 standard; protein; 157 AA.

XX AEB45434;

XX 22-SEP-2005 (first entry)

XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:18.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;

KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
 XX
 XX MPI; 2005-506850/51.
 DR N-PSDB; AEB45446.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 4; SEQ ID NO 18; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;
 Query Match 97.9%; Score 764; DB 1; Length 157;
 Best Local Similarity 94.9%; Pred. No. 0;
 Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;
 Qy 1 VRSSSRTPSDXPVAVHVNANPQAEQLQWLNRRANALLANGVELRDNLQVPSGLYLIYS 60
 Db 1 VRSSSRTPSDMPVAVHVNANPQAEQLQWLNRRANALLANGVELRDNLQVPSGLYLIYS 60
 Qy 61 QVLFEGGCPSTHLLTHTISRIAVSVQTXNLLSAIXSPQRTTPGAEAXPWPEIYL 120
 Db 61 QVLFEGGCPSTHLLTHTISRIAVSVQTXNLLSAIXSPQRTTPGAEAXPWPEIYL 120
 Qy 121 GGVFQLEKGRDLRLAEINRPNVLDLPAESQGVYFGIALL 157
 Db 121 GGVFQLEKGRDLRLAEINRPNVLDLPAESQGVYFGIALL 157

RESULT 6
 AEB45430
 ID AEB45430 standard; protein; 157 AA.
 XX
 AC AEB45430;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:14.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
 XX
 XX MPI; 2005-506850/51.
 DR N-PSDB; AEB45444.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 4; SEQ ID NO 14; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX

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SQ      Sequence 157 AA;
Query Match      97.7%; Score 762; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 2; Mismatches 7; Indels 0; Gaps 0;
Qy      1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db      1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Qy      61 QVLFPGQCPSTHVLTHTRISIAVSQTXNLLSAIXSPQRETPEGAEAXPWVEPIYL 120
Db      61 QVLFPGQCPSTHVLTHTRISIAVSQTXNLLSAIXSPQRETPEGAEAXPWVEPIYL 120
Qy      61 QVLFPGQCPSTHVLTHTRISIAVSQTXNLLSAIXSPQRETPEGAEAXPWVEPIYL 120
Db      61 QVLFPGQCPSTHVLTHTRISIAVSQTXNLLSAIXSPQRETPEGAEAXPWVEPIYL 120
Qy      121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIALL 157
Db      121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIALL 157
Qy      121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIALL 157
Db      121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 7
AEB45453
ID      AEB45453 standard; protein; 157 AA.
XX      AEB45453;
XX      AC
XX      AEB45453;
DT      22-SEP-2005 (first entry)
XX      TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:37.
XX      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW      antiinflammatory; cytostatic; antiarthritis; antiallergic;
KW      antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mitein.
XX      Homo sapiens.
XX      Synthetic.
XX      WO2005066206-A1.
XX      21-JUL-2005.
XX      05-JAN-2005; 2005WO-JP0000032.
XX      06-JAN-2004; 2004JP-00001427.
XX      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX      (MAYU/) MAYUMI T.
XX      (TSUT/) TSUTSUMI Y.
XX      (NAKA/) NAKAGAWA S.
XX      Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
XX      WPI, 2005-506850/51.
XX      N-PSDB; AEB45476.
XX      Novel tumor necrosis factor TNF mutant protein, useful for treating
PT      and/or preventing diseases such as inflammation, and other diseases
PT      caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT      rheumatoid arthritis, allergy.
XX      Claim 5; SEQ ID NO 37; 34pp; Japanese.
XX      The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC      particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC      TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC      a TNF mutant protein comprising an amino acid sequence derived from the
CC      human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC      one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the

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CC      N-terminus, and amino acid residues at positions 84-89 by other amino
CC      acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC      mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC      protein. The TNF mutant proteins are useful for treating and/or
CC      preventing diseases such as inflammation, and other diseases caused by
CC      overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC      cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC      Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC      transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC      respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC      lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC      etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC      represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC      The sequence data for this patent did not form part of the printed
CC      specification, but was obtained in electronic format directly from WIPO
CC      at ftp.wipo.int/pub/published_pct_sequences.
XX      Sequence 157 AA;
Query Match      97.3%; Score 759; DB 1; Length 157;
Best Local Similarity 94.9%; Pred. No. 0;
Matches 149; Conservative 0; Mismatches 8; Indels 0; Gaps 0;
Qy      1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Db      1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
Qy      61 QVLFPGQCPSTHVLTHTRISIAVSQTXNLLSAIXSPQRETPEGAEAXPWVEPIYL 120
Db      61 QVLFPGQCPSTHVLTHTRISIAVSQTXNLLSAIXSPQRETPEGAEAXPWVEPIYL 120
Qy      121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIALL 157
Db      121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIALL 157

RESULT 8
AEB45431
ID      AEB45431 standard; protein; 157 AA.
XX      AEB45431;
XX      AC
XX      AEB45431;
DT      22-SEP-2005 (first entry)
XX      TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:15.
XX      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW      antiinflammatory; cytostatic; antiarthritis; antiallergic;
KW      antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mitein.
XX      Homo sapiens.
XX      Synthetic.
XX      WO2005066206-A1.
XX      21-JUL-2005.
XX      05-JAN-2005; 2005WO-JP0000032.
XX      06-JAN-2004; 2004JP-00001427.
XX      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX      (MAYU/) MAYUMI T.
XX      (TSUT/) TSUTSUMI Y.
XX      (NAKA/) NAKAGAWA S.
XX      Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;

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XX DR WPI; 2005-506850/51.
XX DR N-PSDB; AEB45445.
XX
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX
XX PS Claim 4; SEQ ID NO 15; 34pp; Japanese.
XX
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX SQ Sequence 157 AA;

Query Match 97.2%; Score 758; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 0; Mismatches 9; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
DB 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

QY 61 QVLFXGGGCPSTHLLTHTTISRIVSYQTQVNVLLSAIXSPCQRETPGAEAXPWYEPYIL 120
DB 61 QVLFSGGCGPSTHLLTHTTISRIVSYQTQVNVLLSAIXSPCQRETPGAEAXPWYEPYIL 120

QY 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIALL 157
DB 121 GGVFQLEPGDRLSAEINRPDYLDPAESGQVYFGIALL 157

RESULT 9
AEB45454
ID AEB45454 standard; protein; 157 AA.
XX
XX AC AEB45454;
XX
XX DT 22-SEP-2005 (first entry)
XX
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:38.
XX
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX KW antiinflammatory; cytostatic; antirheumatic; antirheumatic; antiallergic;
XX KW antiproliferative; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; neurotropic;
XX KW muten.

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OS Homo sapiens.
OS Synthetic.
XX PN WO2005066206-A1.
XX
XX PD 21-JUL-2005.
XX
XX PF 05-JAN-2005; 2005WO-JP000032.
XX
XX PR 06-JAN-2004; 2004JP-00001427.
XX
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX
XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX DR WPI; 2005-506850/51.
XX DR N-PSDB; AEB45477.
XX
XX CC Novel tumor necrosis factor TNF mutant protein, useful for treating
XX CC and/or preventing diseases such as inflammation, and other diseases
XX CC caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX CC rheumatoid arthritis, allergy.
XX
XX PS Claim 5; SEQ ID NO 38; 34pp; Japanese.
XX
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX SQ Sequence 157 AA;

Query Match 96.7%; Score 754; DB 1; Length 157;
Best Local Similarity 94.3%; Pred. No. 0;
Matches 148; Conservative 0; Mismatches 9; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
DB 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

QY 61 QVLFXGGGCPSTHLLTHTTISRIVSYQTQVNVLLSAIXSPCQRETPGAEAXPWYEPYIL 120
DB 61 QVLFSGGCGPSTHLLTHTTISRIVSYQTQVNVLLSAIXSPCQRETPGAEAXPWYEPYIL 120

QY 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIALL 157
DB 121 GGVFQLEPGDRLSAEINRPDYLDPAESGQVYFGIALL 157

RESULT 10
AEB45469
ID AEB45469 standard; protein; 157 AA.

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XX AC AEB45469;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:53.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
XX KW antiinflammatory; cycostatic; antirheumatic; antiarthritis; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW mitein.
XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX DR N-PSDB; AEB45492.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX PS Claim 5; SEQ ID NO 53; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX CC Sequence 157 AA;
XX CC Query Match 96.4%; Score 752; DB 1; Length 157;
XX CC Best Local Similarity 93.6%; Pred. No. 0;
XX CC Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

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QY 1 VRSSRTSPDXPAHVAVANPQAEQQLWLNRRNALLANGVELRDNLVPSSEGLYLYS 60
DB 1 VRSSRTSPDXPAHVAVANPQAEQQLWLNRRNALLANGVELRDNLVPSSEGLYLYS 60
QY 61 QVLFKGGCSTHLLTHTTSRIASVQTXXNLISAIKSPCORETPEGAEAXPWYEPYVL 120
DB 61 QVLFSGGCGCSTHLLTHTTSRIKTSYKPVNLLSAIRSPCORETPEGAEANPWYEPYVL 120
QY 121 GGVFLQEXGDRLSAEINRPDYLDFAESQVYFGIIAL 157
DB 121 GGVFLQEPGDELSAEINRPDYLDFAESQVYFGIIAL 157
RESULT 11
AEB45438
ID AEB45438 standard; protein; 157 AA.
XX AC AEB45438;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:22.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
XX KW antiinflammatory; cycostatic; antirheumatic; antiarthritis; antiallergic;
XX KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX KW vasotropic; cerebroprotective; dermatological; immunomodulator;
XX KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX KW mitein.
XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX DR N-PSDB; AEB45452.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX PS Claim 4; SEQ ID NO 22; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by

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CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX
 SQ Sequence 157 AA;

Query Match 96.3%; Score 751; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFKGGCGPSTHLLTHTTISRIVSVQTXVNLISAIKSPQCRTPGAEAXPWYEPYIL 120
 DB 61 QVLFSGGCGPSTHLLTHTTISRIGPYQRPVNLISAIKSPQCRTPGAEANPWYEPYIL 120
 QY 121 GGVPQLXGDRLSAEINRPDYLDPFASGGQVYFGIIAL 157
 DB 121 GGVPQLXGDRLSAEINRPDYLDPFASGGQVYFGIIAL 157

RESULT 12
 AEB45436
 ID AEB45436 standard; protein; 157 AA.

XX AC AEB45436;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:20.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiproliferative; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX
 XX Homo sapiens.
 OS Synthetic.
 OS
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU)/ MAYUMI T.
 PA (TSUT)/ TSUTSUMI Y.
 PA (NAKA)/ NAKAGAWA S.
 XX
 XX Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45450.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating

PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.

XX
 XX Claim 4; SEQ ID NO 20; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins.
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, cachexia,
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX
 SQ Sequence 157 AA;

Query Match 96.3%; Score 751; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTPSDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTPSDMPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFKGGCGPSTHLLTHTTISRIVSVQTXVNLISAIKSPQCRTPGAEAXPWYEPYIL 120
 DB 61 QVLFSGGCGPSTHLLTHTTISRIGPYQRPVNLISAIKSPQCRTPGAEANPWYEPYIL 120
 QY 121 GGVPQLXGDRLSAEINRPDYLDPFASGGQVYFGIIAL 157
 DB 121 GGVPQLXGDRLSAEINRPDYLDPFASGGQVYFGIIAL 157

RESULT 13
 AEB45461
 ID AEB45461 standard; protein; 157 AA.

XX AC AEB45461;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:45.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antiproliferative; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX
 XX Homo sapiens.
 OS Synthetic.
 OS
 PN WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU)/ MAYUMI T.
 PA (TSUT)/ TSUTSUMI Y.
 PA (NAKA)/ NAKAGAWA S.
 XX
 XX Mayumi T, Teutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45450.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating

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PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP000032.
PR
PR 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45484.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 45; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
XX SQ Sequence 157 AA;
XX
XX Query Match 96.3%; Score 751; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 3; Mismatches 8; Indels 0; Gaps 0;
XX
XX Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
XX Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
XX
XX Qy 61 QVLFKGCQCPSTHLLTHTTISRIASVYCTXNLLSAIXSPCORETPEGAEAPWYEPYIL 120
XX Db 61 QVLFSGQGCPSHLLTHTTISRISAYSAPNLLSAIRSPCORETPEGAEANPWYEPYIL 120
XX
XX Qy 121 GGVFOLEXGDRLSAENRPDYLDFAESGVYFGIIAL 157
XX Db 121 GGVFOLEFGDRLSAENRPDYLDFAESGVYFGIIAL 157
XX
XX RESULT 14
XX ID AEB45460
XX ID AEB45460 standard; protein; 157 AA.
XX
XX AC AEB45460;
XX
XX DT 22-SEP-2005 (first entry)
XX
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DE
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; anticrheumatic; antiarthritic; aniallergic;
XX antiproliferative; anti-HIV; antiatherosclerotic; immunosuppressive;
XX vasotropic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.
XX
XX Homo sapiens.
XX Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45483.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 5; SEQ ID NO 44; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX SQ Sequence 157 AA;
XX
XX Query Match 96.2%; Score 750; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
XX
XX Qy 1 VRSSRTPSDXPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
XX Db 1 VRSSRTPSDMPVAHVANPQAEQQLWLNRRANALLANGVELRDNLQVWPSGLYLIYS 60
XX
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Qy 61 QVLPXGCGCPSTHVLTHTRISAVSYQTWNLSAIXSPCQRETPGAGAXPWYEPYIL 120
 Db 61 QVLPXGCGCPSTHVLTHTRISAVSYQTWNLSAIXSPCQRETPGAGAXPWYEPYIL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGGVYFGIIAL 157
 Db 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGGVYFGIIAL 157

RESULT 15
 AEB45464
 ID AEB45464 standard; protein; 157 AA.
 XX
 AC AEB45464;
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:48.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmidium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYS) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
 XX
 DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45487.
 XX
 PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 5; SEQ ID NO 48; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins,
 particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 a TNF mutant protein comprising an amino acid sequence derived from the
 human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 N-terminus, and amino acid residues at positions 84-89 by other amino
 acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 mutant protein; and (2) a TNF formulation comprising a TNF mutant
 protein. The TNF mutant proteins are useful for treating and/or
 preventing diseases such as inflammation, and other diseases caused by
 overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 cancer, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic

CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 96.2%; Score 750; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSRTPSDXPAHVAVNPQAEGLQWLNRNALLANGVELRDNLQVVPSEGLYLIYS 60
 Db 1 VRSSRTPSDMPVAVVAVNPQAEGLQWLNRNALLANGVELRDNLQVVPSEGLYLIYS 60
 Qy 61 QVLPXGCGCPSTHVLTHTRISAVSYQTWNLSAIXSPCQRETPGAGAXPWYEPYIL 120
 Db 61 QVLPXGCGCPSTHVLTHTRISAVSYQTWNLSAIXSPCQRETPGAGAXPWYEPYIL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGGVYFGIIAL 157
 Db 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGGVYFGIIAL 157

RESULT 16
 AEB45472
 ID AEB45472 standard; protein; 157 AA.
 AC AEB45472;
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:56.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmidium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYS) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 PI Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
 XX
 DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45495.
 XX
 PT Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 PS Claim 5; SEQ ID NO 56; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.

XX Sequence 157 AA;

Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
Qy 61 QVLFPGQCPSTHVLTTHTISRIAVSYQTVNLLSAIXSPQRETPEGAEXPWVEPIYL 120
Db 61 QVLFSGQCPSTHVLTTHTISRIKSYGHPVNLLSAIRSPQRETPEGAEXPWVEPIYL 120
Qy 121 GGVOLEXGDRLSAENRPDYLDPAESGVYFGIALL 157
Db 121 GGVOLEPGDRLSAENRPDYLDPAESGVYFGIALL 157

RESULT 17
AEB45471
ID AEB45471 standard; protein; 157 AA.
XX
AC AEB45471;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:55.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmoidium infection; meningitis; hepatitis; Alzhimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritis; antiallergic;
KW antipsoriatic; anti-Hiv; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatoclerotic; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutin.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO200506206-A1.
XX
PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
PR 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Teutsuami Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45494.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
PS Claim 5; SEQ ID NO 55; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX Sequence 157 AA;
Qy Query Match 96.0%; Score 749; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDXPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
Db 1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVWPSGLYLIYS 60
Qy 61 QVLFPGQCPSTHVLTTHTISRIAVSYQTVNLLSAIXSPQRETPEGAEXPWVEPIYL 120
Db 61 QVLFSGQCPSTHVLTTHTISRIPTGPPVNLLSAIRSPQRETPEGAEXPWVEPIYL 120
Qy 121 GGVOLEXGDRLSAENRPDYLDPAESGVYFGIALL 157
Db 121 GGVOLEPGDRLSAENRPDYLDPAESGVYFGIALL 157
RESULT 18
AEB45455
ID AEB45455 standard; protein; 157 AA.
XX
AC AEB45455;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:39.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;

KW plasmodium infection; meningitis; hepatitis; antirheumatic; antiarthritic; antiallergic;
 KW antiinflammatory; cytostatic; antitumor; severe acute respiratory syndrome;
 KW antiparasitic; anti-HIV; antituberculous; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 XX W02005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX (MAYU/) MAYUMI T.
 XX (TSUT/) TSUTSUMI Y.
 XX (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX N-PSDB; AEB45478.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 XX and/or preventing diseases such as inflammation, and other diseases
 XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
 XX rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 39; 34pp; Japanese.
 XX
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 XX a TNF mutant protein comprising an amino acid sequence derived from the
 XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 XX N-terminus, and amino acid residues at positions 84-89 by other amino
 XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
 XX protein. The TNF mutant proteins are useful for treating and/or
 XX preventing diseases such as inflammation, and other diseases caused by
 XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
 XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 XX The sequence data for this patent did not form part of the printed
 XX specification, but was obtained in electronic format directly from WIPO
 XX at ftp.wipo.int/pub/published_pct_sequences.

Query Match 96.0%; Score 749; DB 1; Length 157;
 Best Local Similarity 93.6%; Pred. No. 0;
 Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;
 QY 1 VRSSRRPSPDXPAHVAVNPAEQQLWLNRRANALLANGVELNDNLVPSSEGLYLIS 60
 DB 1 VRSSRRPSPDXPAHVAVNPAEQQLWLNRRANALLANGVELNDNLVPSSEGLYLIS 60
 QY 61 QVLFPGGCPSTHLLTHTISRIASVYQTQVNLISATSPQCRTPGAEANPWYPIYL 120
 DB 61 QVLFPGGCPSTHLLTHTISRIASVYQTQVNLISATSPQCRTPGAEANPWYPIYL 120
 - QY 121 GGVFQLEKXGDRLSAEINRPDYLDFAARGQVYFGIALL 157

Db 121 GGVFQLEKXGDRLSAEINRPDYLDFAARGQVYFGIALL 157
 RESULT 19
 AEB45466
 ID AEB45466 standard; protein; 157 AA.
 XX
 AC AEB45466;
 XX
 XX 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:50.
 XX
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antituberculous;
 KW antiparasitic; anti-HIV; antituberculous; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutin.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 XX W02005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 XX (MAYU/) MAYUMI T.
 XX (TSUT/) TSUTSUMI Y.
 XX (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX WPI; 2005-506850/51.
 XX N-PSDB; AEB45489.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 XX and/or preventing diseases such as inflammation, and other diseases
 XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
 XX rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 50; 34pp; Japanese.
 XX
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 XX a TNF mutant protein comprising an amino acid sequence derived from the
 XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 XX N-terminus, and amino acid residues at positions 84-89 by other amino
 XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
 XX protein. The TNF mutant proteins are useful for treating and/or
 XX preventing diseases such as inflammation, and other diseases caused by
 XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
 XX represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 XX The sequence data for this patent did not form part of the printed
 XX specification, but was obtained in electronic format directly from WIPO


```

CC at ftp.wipo.int/pub/published_pct_sequences.
XX Sequence 157 AA;
SQ
    Query Match          96.0%; Score 749; DB 1; Length 157;
    Best Local Similarity 93.0%; Pred. No. 0;
    Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
QY 1 VRSSRTPSDXPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
DB 1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
QY 61 QVLFQXGQCPSTHLLTHTISRIAVSYQTXNLSAIXSPQRETPEGAEXPWYEPYIL 120
DB 61 QVLFSGQGPCSTHLLTHTISRIKSYGHPVNLLSAIRSPQRETPEGAEXPWYEPYIL 120
QY 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
DB 121 GGVFQLEPGRDLSAEINRPDYLDFAESGQVYFGIIAL 157
RESULT 20
AEB45474
ID AEB45474 standard; protein; 157 AA.
XX
AC AEB45474;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:58.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mitein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
DR N-PSDB; AEB45497.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
PS Claim 5; SEQ ID NO 58; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the

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CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimers disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;
    Query Match          96.0%; Score 749; DB 1; Length 157;
    Best Local Similarity 93.6%; Pred. No. 0;
    Matches 147; Conservative 0; Mismatches 10; Indels 0; Gaps 0;
QY 1 VRSSRTPSDXPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
DB 1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
QY 61 QVLFQXGQCPSTHLLTHTISRIAVSYQTXNLSAIXSPQRETPEGAEXPWYEPYIL 120
DB 61 QVLFSGQGPCSTHLLTHTISRIHRYQDPVNLLSAIRSPQRETPEGAEXPWYEPYIL 120
QY 121 GGVFQLEKXGDRLSAEINRPDYLDFAESGQVYFGIIAL 157
DB 121 GGVFQLEPGRDLSAEINRPDYLDFAESGQVYFGIIAL 157
RESULT 21
AEB45457
ID AEB45457 standard; protein; 157 AA.
XX
AC AEB45457;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:41.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mitein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.

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XX PI Mayumi T, Tautsumi Y, Nakagawa S, Ohta T;
XX OS WPI; 2005-506850/51.
XX PA N-PSDB; AEB45480.
XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
XX PT and/or preventing diseases such as inflammation, and other diseases
XX PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX PT rheumatoid arthritis, allergy.
XX PS Claim 5; SEQ ID NO 41; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;
XX Query Match 96.0%; Score 749; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDKPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFXGQGCPSHTVLLTHTTISRIVSVYQTXVNLLSAIXSPCQRTPEGAEXPWEPIYL 120
Db 61 QVLFSGGQGCPSHTVLLTHTTISRISADYPHPVNLLSAIRSPCQRTPEGAEXPWEPIYL 120
Qy 121 GGVFQLXGDRLSAEINRPDYLDPAESGVYFGIIAL 157
Db 121 GGVFQLFPGDRLSAEINRPDYLDPAESGVYFGIIAL 157
XX RESULT 22
XX AEB45475
XX ID AEB45475 standard; protein; 157 AA.
XX AC AEB45475;
XX XX
XX DT 22-SEP-2005 (first entry)
XX DE
XX XX
XX TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:59.
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; antiarheumatic; antiarthritic; antiallergic;
XX antipeptidic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotrophic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;

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KW mutuin.
XX OS Homo sapiens.
XX PA Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU/) MAYUMI T.
XX PA (TSUT/) TSUTSUMI Y.
XX PA (NAKA/) NAKAGAWA S.
XX PI Mayumi T, Tautsumi Y, Nakagawa S, Ohta T;
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45498.
XX DR Novel tumor necrosis factor TNF mutant protein, useful for treating
XX DR and/or preventing diseases such as inflammation, and other diseases
XX DR caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX DR rheumatoid arthritis, allergy.
XX PS Claim 5; SEQ ID NO 59; 34pp; Japanese.
XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX CC a TNF mutant protein comprising an amino acid sequence derived from the
XX CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX CC N-terminus, and amino acid residues at positions 84-89 by other amino
XX CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX CC protein. The TNF mutant proteins are useful for treating and/or
XX CC preventing diseases such as inflammation, and other diseases caused by
XX CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
XX CC The sequence data for this patent did not form part of the printed
XX CC specification, but was obtained in electronic format directly from WIPO
XX CC at ftp.wipo.int/pub/published_pct_sequences.
XX SQ Sequence 157 AA;
XX Query Match 96.0%; Score 749; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;
Qy 1 VRSSRTPSDKPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTPSDMPVAVHVVANPQAEQQLQWLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFXGQGCPSHTVLLTHTTISRIVSVYQTXVNLLSAIXSPCQRTPEGAEXPWEPIYL 120
Db 61 QVLFSGGQGCPSHTVLLTHTTISRISADYPHPVNLLSAIRSPCQRTPEGAEXPWEPIYL 120
Qy 121 GGVFQLXGDRLSAEINRPDYLDPAESGVYFGIIAL 157
Db 121 GGVFQLFPGDRLSAEINRPDYLDPAESGVYFGIIAL 157
XX RESULT 23

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AEB45458
ID AEB45458 standard; protein; 157 AA.
XX
AC AEB45458;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID NO:42.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW munein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX
DR WPI; 2005-506850/51.
DR N-PSDB; AEB45481.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
PS Claim 5; SEQ ID NO 42; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection (stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.
XX
SQ Sequence 157 AA;
Query Match 95.9%; Score 748; DB 1; Length 157;

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Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;
Qy 1 VRSSRTSPDXPAHVAVNPQAEQQLWLNPRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSRTSPDXPAHVAVNPQAEQQLWLNPRNALLANGVELRDNLVVPSEGLYLIYS 60
Qy 61 QVLFPGQGCSTHVLTHLTISRIASVYOTXVNLLSAIXSPCQRETPEGAAXPWYEPIYL 120
Db 61 QVLFPGQGCSTHVLTHLTISRIASVYOTXVNLLSAIXSPCQRETPEGAAXPWYEPIYL 120
Qy 121 GGVEQLEKGRDLSAEINRPDYLDAESGVYFGIALL 157
Db 121 GGVEQLEKGRDLSAEINRPDYLDAESGVYFGIALL 157
RESULT 24
ID AEB45473 standard; protein; 157 AA.
XX
AC AEB45473;
XX
DT 22-SEP-2005 (first entry)
XX
DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID NO:57.
XX
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW munein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX
DR WPI; 2005-506850/51.
DR N-PSDB; AEB45496.
XX
PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.
XX
PS Claim 5; SEQ ID NO 57; 34pp; Japanese.
XX
CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant

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CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.9%; Score 748; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy 1 VRSSSRTPSDXPFVAHVANPQAEQQLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSSRTPSDMPVAHVANPQAEQQLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQGCSTHLLTHTRISRIASVQTXVNLSSAIXSPCQRTPEGAEXPWYEPYIL 120
Db 61 QVLFPGQGCSTHLLTHTRISRIASVQTXVNLSSAIXSPCQRTPEGAEXPWYEPYIL 120

Qy 121 GGVFQLEPGDRLSAEINRNPDLDPFASGQVYFGIALL 157
Db 121 GGVFQLEPGDRLSAEINRNPDLDPFASGQVYFGIALL 157

RESULT 25
AEB45467
ID AEB45467 standard; protein; 157 AA.

XX AC AEB45467;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:51.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotrophic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.

XX OS Homo sapiens.
XX OS Synthetic.
XX PN WO2005066206-A1.
XX PD 21-JUL-2005.
XX PF 05-JAN-2005; 2005WO-JP000032.
XX PR 06-JAN-2004; 2004JP-00001427.
XX PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
XX PA (MAYU) MAYUMI T.
XX PA (TSUT) TSUTSUMI Y.
XX PA (NAKA) NAKAGAWA S.
XX PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
XX WPI, 2005-506850/51.
XX DR N-P8DB; AEB45490.

XX PT Novel tumor necrosis factor TNF mutant protein, useful for treating
PT and/or preventing diseases such as inflammation, and other diseases
PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
PT rheumatoid arthritis, allergy.

XX PS Claim 5; SEQ ID NO 51; 34pp; Japanese.

XX CC The invention relates to tumor necrosis factor (TNF) mutant proteins,
CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
CC a TNF mutant protein comprising an amino acid sequence derived from the
CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
CC N-terminus, and amino acid residues at positions 84-89 by other amino
CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
CC protein. The TNF mutant proteins are useful for treating and/or
CC preventing diseases such as inflammation, and other diseases caused by
CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC The sequence data for this patent did not form part of the printed
CC specification, but was obtained in electronic format directly from WIPO
CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.9%; Score 748; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 2; Mismatches 9; Indels 0; Gaps 0;

Qy 1 VRSSSRTPSDXPFVAHVANPQAEQQLNRRNALLANGVELRDNLVVPSEGLYLIYS 60
Db 1 VRSSSRTPSDMPVAHVANPQAEQQLNRRNALLANGVELRDNLVVPSEGLYLIYS 60

Qy 61 QVLFPGQGCSTHLLTHTRISRIASVQTXVNLSSAIXSPCQRTPEGAEXPWYEPYIL 120
Db 61 QVLFPGQGCSTHLLTHTRISRIASVQTXVNLSSAIXSPCQRTPEGAEXPWYEPYIL 120

Qy 121 GGVFQLEPGDRLSAEINRNPDLDPFASGQVYFGIALL 157
Db 121 GGVFQLEPGDRLSAEINRNPDLDPFASGQVYFGIALL 157

RESULT 26
AEB45468
ID AEB45468 standard; protein; 157 AA.

XX AC AEB45468;
XX DT 22-SEP-2005 (first entry)
XX DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:52.
XX KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
XX antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
XX vasotrophic; cerebroprotective; dermatological; immunomodulator;
XX antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
XX mutein.

XX OS Homo sapiens.
XX OS Synthetic.


```

Db      1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSSGLYLIYS 60
Qy      61 QVLFXGGGCPSTHLLTHTTISRIVSYQTQVNLISAIKSPCQRETTPGAEAXPWYEPYIL 120
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db      61 QVLFSGGGCPSTHLLTHTTISRITSTHNQPVNLLSAIRSPCQRETTPGAEANPWYEPYIL 120
Qy      121 GGVFQLXGDRLSAEINRPDYLDPAESGGVYFGIIAL 157
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db      121 GGVFQLSPGDRLSAEINRPDYLDPAESGGVYFGIIAL 157

RESULT 28
AEB45462
ID      AEB45462 standard; protein; 157 AA.
XX      AC
XX      AEB45462;
DT      22-SEP-2005 (first entry)
XX      TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:46.
XX      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW      antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      animalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mutein.
XX      Homo sapiens.
OS      Synthetic.
XX      WO2005066206-A1.
XX      PN
XX      PD
XX      21-JUL-2005.
XX      05-JAN-2005; 2005WO-JP000032.
XX      PF
XX      PR
XX      06-JAN-2004; 2004JP-00001427.
XX      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX      PA (MAYU)/ MAYUMI T.
XX      PA (TSUT)/ TSUTSUMI Y.
XX      PA (NAKA)/ NAKAGAWA S.
XX      PI
XX      Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX      WPI; 2005-506850/51.
XX      DR N-PSDB; AEB45485.
XX      Novel tumor necrosis factor TNF mutant protein, useful for treating
XX      and/or preventing diseases such as inflammation, and other diseases
XX      caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX      rheumatoid arthritis, allergy.
XX      Claim 5; SEQ ID NO 46; 34pp; Japanese.
XX      The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX      particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX      TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX      a TNF mutant protein comprising an amino acid sequence derived from the
XX      human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX      one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX      N-terminus, and amino acid residues at positions 84-89 by other amino
XX      acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX      mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX      protein. The TNF mutant proteins are useful for treating and/or
XX      preventing diseases such as inflammation, and other diseases caused by
XX      overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX      cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX      Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,

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CC      transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
CC      respiratory syndrome (SARS), atherosclerosis, Bence's disease, systemic
CC      lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
CC      etc. The TNF mutant proteins are highly stable in vivo. This sequence
CC      represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
CC      The sequence data for this patent did not form part of the printed
CC      specification, but was obtained in electronic format directly from WIPO
CC      at ftp.wipo.int/pub/published_pct_sequences.
XX      SQ
XX      Sequence 157 AA;

```

```

Query Match      95.8%; Score 747; DB 1; Length 157;
Best Local Similarity 93.0%; Pred. No. 0;
Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

Qy      1 VRSSRTPSDXPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSSGLYLIYS 60
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db      1 VRSSRTPSDMPVAHVANPQAEGLQWLNRRANALLANGVELRDNLVVPSSGLYLIYS 60
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :

Qy      61 QVLFXGGGCPSTHLLTHTTISRIVSYQTQVNLISAIKSPCQRETTPGAEAXPWYEPYIL 120
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db      61 QVLFSGGGCPSTHLLTHTTISRITSTHNQPVNLLSAIRSPCQRETTPGAEANPWYEPYIL 120
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :

Qy      121 GGVFQLXGDRLSAEINRPDYLDPAESGGVYFGIIAL 157
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :
Db      121 GGVFQLSPGDRLSAEINRPDYLDPAESGGVYFGIIAL 157
        : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : : :

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RESULT 29
AEB45470
ID      AEB45470 standard; protein; 157 AA.
XX      AC
XX      AEB45470;
DT      22-SEP-2005 (first entry)
XX      DE
XX      TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:54.
XX      tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW      autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW      acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW      plasmodium infection; meningitis; hepatitis; Alzheimers disease;
KW      antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW      antipneumatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW      vasotropic; cerebroprotective; dermatological; immunomodulator;
KW      animalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW      mutein.
XX      Homo sapiens.
OS      Synthetic.
XX      WO2005066206-A1.
XX      PD
XX      21-JUL-2005.
XX      PF
XX      05-JAN-2005; 2005WO-JP000032.
XX      PR
XX      06-JAN-2004; 2004JP-00001427.
XX      (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX      PA (MAYU)/ MAYUMI T.
XX      PA (TSUT)/ TSUTSUMI Y.
XX      PA (NAKA)/ NAKAGAWA S.
XX      PI
XX      Mayumi T, Teutsuimi Y, Nakagawa S, Ohta T;
XX      WPI; 2005-506850/51.
XX      DR N-PSDB; AEB45493.
XX      Novel tumor necrosis factor TNF mutant protein, useful for treating
XX      and/or preventing diseases such as inflammation, and other diseases
XX      caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX      rheumatoid arthritis, allergy.

```


autoimmunity disease; tumor; transplant rejection; cardiovascular disease; acquired immune deficiency syndrome; severe acute respiratory syndrome; plasmid infection; meningitis; hepatitis; Alzheimer's disease; anti-inflammatory; cytotoxic; antineoplastic; antitumor; anti-allergic; anti-HIV; anti-arteriosclerotic; immunosuppressive; vasotropic; cerebroprotective; dermatological; immunomodulator; antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic; mitein.

Homo sapiens.
 Synthetic.
 WO2005066206-A1.
 21-JUL-2005.
 05-JAN-2005; 2005WO-JP000032.
 06-JAN-2004; 2004JP-00001427.
 (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 (MAYU) MAYUMI T.
 (TSUT) TSUTSUMI Y.
 (NAKA) NAKAGAWA S.
 Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 WPI; 2005-506850/51.
 N-PSDB; AEB45482.

Novel tumor necrosis factor TNF mutant protein, useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.

Claim 5; SEQ ID NO 43; 34pp; Japanese.

The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R2. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

Query Match
 Best Local Similarity 95.6%; Score 746; DB 1; Length 157;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTPSDPVAVHVNPAEQQLWLNRRALLANGVELDQNLVPSGGLYLIYS 60
 DB 1 VRSSRTPSDPVAVHVNPAEQQLWLNRRALLANGVELDQNLVPSGGLYLIYS 60
 QY 61 QVLFKGGCPTHTLLTHITIRIAVSQYQTNLLSAXSPQRTTPEGAXPWPVEPIYL 120
 DB 61 QVLFKGGCPTHTLLTHITIRIAVSQYQTNLLSAXSPQRTTPEGAXPWPVEPIYL 120

QY 121 GGVFQLEXGDRLSAEINRRPDYLDPAESGQVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRRPDYLDPAESGQVYFGIIAL 157

RESULT 32
 AEB45465
 ID AEB45465 standard; protein; 157 AA.
 XX
 AC AEB45465;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:49.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation; autoimmunity disease; tumor; transplant rejection; cardiovascular disease; acquired immune deficiency syndrome; severe acute respiratory syndrome; plasmid infection; meningitis; hepatitis; Alzheimer's disease; anti-inflammatory; cytotoxic; antineoplastic; antitumor; anti-allergic; anti-HIV; anti-arteriosclerotic; immunosuppressive; vasotropic; cerebroprotective; dermatological; immunomodulator; antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic; mitein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 PN WO2005066206-A1.
 XX
 PD 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU) MAYUMI T.
 PA (TSUT) TSUTSUMI Y.
 PA (NAKA) NAKAGAWA S.
 XX
 PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 XX
 DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45488.
 XX
 PT Novel tumor necrosis factor TNF mutant protein, useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumor, rheumatoid arthritis, allergy.
 PT
 PT
 PT
 PT
 PS Claim 5; SEQ ID NO 49; 34pp; Japanese.
 XX
 CC The invention relates to tumor necrosis factor (TNF) mutant proteins, particularly tumor necrosis factor mutant proteins specific for TNF-R1 or TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses a TNF mutant protein comprising an amino acid sequence derived from the human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the N-terminus, and amino acid residues at positions 84-89 by other amino acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF mutant protein; and (2) a TNF formulation comprising a TNF mutant protein. The TNF mutant proteins are useful for treating and/or preventing diseases such as inflammation, and other diseases caused by overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma), Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia, transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease, etc. The TNF mutant proteins are highly stable in vivo. This sequence represents a human TNF-alpha mutant protein specific for TNF-R2. Note: The sequence data for this patent did not form part of the printed specification, but was obtained in electronic format directly from WIPO at ftp.wipo.int/pub/published_pct_sequences.

CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;

QY 1 VRSSRTPSDYPAHVAVNPAEQQLWLNRRNALLANGVELRDNLVPSGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVAVNPAEQQLWLNRRNALLANGVELRDNLVPSGLYLIYS 60
 QY 61 QVLFSGQGPCSTHVLTTHTTISRIVSYQTXVNLLSAIXSPCQRETPEGAEXPWEPIYL 120
 DB 61 QVLFSGQGPCSTHVLTTHTTISRIVSYQTXVNLLSAIXSPCQRETPEGAEXPWEPIYL 120
 QY 121 GGVFQLEXGDRLSAENRPNPDYLDFAESGQVYFGIALL 157
 DB 121 GGVFQLEPGDRLSAENRPNPDYLDFAESGQVYFGIALL 157

RESULT 33
 AEB45463
 ID AEB45463 standard; protein; 157 AA.
 XX
 AC AEB45463;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R2 specific human TNF-alpha mutant protein, SEQ ID No:47.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmoidium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipapillary; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO200506206-A1.
 XX
 PD 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP0000032.
 XX
 PF 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
 FI WPI; 2005-506850/51.
 XX
 DR N-PSDB; AEB45486.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 5; SEQ ID NO 47; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or

CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Bence's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimers disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R2. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 SQ Sequence 157 AA;

Query Match 95.6%; Score 746; DB 1; Length 157;
 Best Local Similarity 93.0%; Pred. No. 0;
 Matches 146; Conservative 1; Mismatches 10; Indels 0; Gaps 0;

QY 1 VRSSRTPSDYPAHVAVNPAEQQLWLNRRNALLANGVELRDNLVPSGLYLIYS 60
 DB 1 VRSSRTPSDMPVAHVAVNPAEQQLWLNRRNALLANGVELRDNLVPSGLYLIYS 60
 QY 61 QVLFSGQGPCSTHVLTTHTTISRIVSYQTXVNLLSAIXSPCQRETPEGAEXPWEPIYL 120
 DB 61 QVLFSGQGPCSTHVLTTHTTISRIVSYQTXVNLLSAIXSPCQRETPEGAEXPWEPIYL 120
 QY 121 GGVFQLEXGDRLSAENRPNPDYLDFAESGQVYFGIALL 157
 DB 121 GGVFQLEPGDRLSAENRPNPDYLDFAESGQVYFGIALL 157

RESULT 34
 AEB45429
 ID AEB45429 standard; protein; 157 AA.
 XX
 AC AEB45429;
 XX
 DT 22-SEP-2005 (first entry)
 XX
 DE TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:13.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmoidium infection; meningitis; hepatitis; Alzheimers disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipapillary; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotrophic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.
 XX
 OS Homo sapiens.
 OS Synthetic.
 XX
 PN WO200506206-A1.
 XX
 PD 21-JUL-2005.
 XX
 PF 05-JAN-2005; 2005WO-JP0000032.
 XX
 PR 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.

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PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45443.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 13; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 95.4%; Score 744; DB 1; Length 157;
XX Best Local Similarity 93.0%; Pred. No. 0;
XX Matches 146; Conservative 0; Mismatches 11; Indels 0; Gaps 0;
XX
XX Qy 1 VRSSRTSPDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
XX Db 1 VRSSRTSPDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
XX
XX Qy 61 QVLFKXGQCPSTHVLTHTTISRIAVSYQTQXVNLISAIKSPQRTPEGAEXPWYEPYIL 120
XX Db 61 QVLFKXGQCPSTHVLTHTTISRIAVSYQTQXVNLISAIKSPQRTPEGAEXPWYEPYIL 120
XX
XX Qy 121 GGVFQLEKXGDRLSAEINRNPDLDPFAGSQVYFGIALL 157
XX Db 121 GGVFQLEKXGDRLSAEINRNPDLDPFAGSQVYFGIALL 157
XX
XX RESULT 35
XX AEB45428
XX ID AEB45428 standard; protein, 157 AA.
XX
XX AC AEB45428;
XX
XX XX 22-SEP-2005 (first entry)
XX
XX XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:12.
XX
XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
XX autoimmune disease; tumor; transplant rejection; cardiovascular disease;
XX acquired immune deficiency syndrome; severe acute respiratory syndrome;
XX plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
XX anti-inflammatory; cytostatic; antirheumatic; antithratic; antiallergic;
XX antiparasitic; anti-HIV; antiarteriosclerotic; immunosuppressive;

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KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
XX Homo sapiens.
XX Synthetic.
XX
XX WO2005066206-A1.
XX
XX 21-JUL-2005.
XX
XX 05-JAN-2005; 2005WO-JP000032.
XX
XX 06-JAN-2004; 2004JP-00001427.
XX
XX (HAYB ) HAYASHIBARA SEIBUTSU KAGAKU.
XX (MAYU/) MAYUMI T.
XX (TSUT/) TSUTSUMI Y.
XX (NAKA/) NAKAGAWA S.
XX
XX Mayumi T, Teutsami Y, Nakagawa S, Ohta T;
XX
XX WPI; 2005-506850/51.
XX N-PSDB; AEB45442.
XX
XX Novel tumor necrosis factor TNF mutant protein, useful for treating
XX and/or preventing diseases such as inflammation, and other diseases
XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
XX rheumatoid arthritis, allergy.
XX
XX Claim 4; SEQ ID NO 12; 34pp; Japanese.
XX
XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
XX a TNF mutant protein comprising an amino acid sequence derived from the
XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
XX N-terminus, and amino acid residues at positions 84-89 by other amino
XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
XX protein. The TNF mutant proteins are useful for treating and/or
XX preventing diseases such as inflammation, and other diseases caused by
XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
XX cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
XX Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
XX transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
XX respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
XX lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
XX etc. The TNF mutant proteins are highly stable in vivo. This sequence
XX represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
XX The sequence data for this patent did not form part of the printed
XX specification, but was obtained in electronic format directly from WIPO
XX at ftp.wipo.int/pub/published_pct_sequences.
XX
XX Sequence 157 AA;
XX
XX Query Match 95.3%; Score 743; DB 1; Length 157;
XX Best Local Similarity 92.4%; Pred. No. 0;
XX Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;
XX
XX Qy 1 VRSSRTSPDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
XX Db 1 VRSSRTSPDXPVAVHVVANPQAEQQLWLNRRNALLANGVELRDNLQVPSGLYLIYS 60
XX
XX Qy 61 QVLFKXGQCPSTHVLTHTTISRIAVSYQTQXVNLISAIKSPQRTPEGAEXPWYEPYIL 120
XX Db 61 QVLFKXGQCPSTHVLTHTTISRIAVSYQTQXVNLISAIKSPQRTPEGAEXPWYEPYIL 120
XX
XX Qy 121 GGVFQLEKXGDRLSAEINRNPDLDPFAGSQVYFGIALL 157
XX Db 121 GGVFQLEKXGDRLSAEINRNPDLDPFAGSQVYFGIALL 157

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RESULT 36
AEB45425
ID AEB45425 standard; protein; 157 AA.
XX
AC AEB45425;
XX
DT 22-SEP-2005 (first entry)
XX
TNF-R1 specific human TNF-alpha mutant protein, SEQ ID NO:9.
DE
KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP0000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
PI WPI; 2005-506850/51.
PI N-PSDB; AEB45439.
DR
XX
Novel tumor necrosis factor TNF mutant protein, useful for treating
and/or preventing diseases such as inflammation, and other diseases
caused by overexpression of TNF, such as autoimmune diseases, tumor,
rheumatoid arthritis, allergy.
XX
PS Claim 4; SEQ ID NO 9; 34pp; Japanese.
XX
The invention relates to tumor necrosis factor (TNF) mutant proteins,
particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
a TNF mutant protein comprising an amino acid sequence derived from the
human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
N-terminus, and amino acid residues at positions 84-89 by other amino
acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
mutant protein; and (2) a TNF formulation comprising a TNF mutant
protein. The TNF mutant proteins are useful for treating and/or
preventing diseases such as inflammation, and other diseases caused by
overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
etc. The TNF mutant proteins are highly stable in vivo. This sequence
represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
The sequence data for this patent did not form part of the printed
specification, but was obtained in electronic format directly from WIPO
at ftp.wipo.int/pub/published_pct_sequences.
XX
Sequence 157 AA;

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Query Match 95.3%; Score 743; DB 1; Length 157;
Best Local Similarity 92.4%; Pred. No. 0;
Matches 145; Conservative 2; Mismatches 10; Indels 0; Gaps 0;
QY 1 VRSSRTPSDYPAHVAVNPAEQQLWLNRRANALLANGVELRDNLVPSGGLYLYS 60
DB 1 VRSSRTPSDMPVAHVAVNPAEQQLWLNRRANALLANGVELRDNLVPSGGLYLYS 60
QY 61 QVLFXGQGCPTTHVLLTHTISRIVSVYQTXVNLISAIXSPCQRETPEGAEXPWYEPIYL 120
DB 61 QVLFXGQGCPTTHVLLTHTISRIVSVYQTXVNLISAIXSPCQRETPEGAEXPWYEPIYL 120
QY 121 GGVFQLEXGDRLSAEINRPDYLDFAESGQVYFGIALL 157
DB 121 GGVFQLEXGDRLSAEINRPDYLDFAESGQVYFGIALL 157
RESULT 37
AEB45421
ID AEB45421 standard; protein; 157 AA.
XX
AC AEB45421;
XX
DT 22-SEP-2005 (first entry)
XX
Human TNF-alpha mutant protein, SEQ ID No:5.
XX
tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
KW plasmoidium infection; meningitis; hepatitis; Alzheimer's disease;
KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
KW vasotropic; cerebroprotective; dermatological; immunomodulator;
KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
KW mutein.
XX
OS Homo sapiens.
OS Synthetic.
XX
PN WO2005066206-A1.
XX
PD 21-JUL-2005.
XX
PF 05-JAN-2005; 2005WO-JP0000032.
XX
PR 06-JAN-2004; 2004JP-00001427.
XX
PA (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
PA (MAYU/) MAYUMI T.
PA (TSUT/) TSUTSUMI Y.
PA (NAKA/) NAKAGAWA S.
XX
PI Mayumi T, Tsutsumi Y, Nakagawa S, Ohta T;
PI WPI; 2005-506850/51.
PI N-PSDB; AEB45422.
XX
Novel tumor necrosis factor TNF mutant protein, useful for treating
and/or preventing diseases such as inflammation, and other diseases
caused by overexpression of TNF, such as autoimmune diseases, tumor,
rheumatoid arthritis, allergy.
XX
PS Example 1; SEQ ID NO 5; 34pp; Japanese.
XX
The invention relates to tumor necrosis factor (TNF) mutant proteins,
particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
a TNF mutant protein comprising an amino acid sequence derived from the
human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
N-terminus, and amino acid residues at positions 84-89 by other amino
acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
mutant protein; and (2) a TNF formulation comprising a TNF mutant
protein. The TNF mutant proteins are useful for treating and/or
preventing diseases such as inflammation, and other diseases caused by
overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
etc. The TNF mutant proteins are highly stable in vivo. This sequence
represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
The sequence data for this patent did not form part of the printed
specification, but was obtained in electronic format directly from WIPO
at ftp.wipo.int/pub/published_pct_sequences.
XX
Sequence 157 AA;

```

CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents human TNF-alpha mutant protein. Note: The sequence data for
 CC this patent did not form part of the printed specification, but was
 CC obtained in electronic format directly from WIPO at
 CC ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.1%; Score 742; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;
 QY 1 VRSSRTSPDXPVAVHVNPAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 DB 1 VRSSRTSPDMPVAVHVNPAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60
 QY 61 QVLFQXGQCPSTHLLTHTTISRIVSYQTPVNLSSAIXSPCQRETPGABAXPWYEPYIL 120
 DB 61 QVLFQXGQCPSTHLLTHTTISRIVSYQTPVNLSSAIXSPCQRETPGABAXPWYEPYIL 120
 QY 121 GGVFQLEPGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
 DB 121 GGVFQLEPGDRLSAEINRPDYLDPFXXXGQVYFGIIAL 157

RESULT 38

AEBA45427
 ID AEB45427 standard; protein; 157 AA.

XX AC AEB45427;

DT 22-SEP-2005 (first entry)

XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:11.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX Homo sapiens.
 OS Synthetic.

XX WO2005066206-A1.

XX 21-JUL-2005.

XX 05-JAN-2005; 2005WO-JP000032.

XX 06-JAN-2004; 2004JP-00001427.

XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.

XX Mayumi T, Teatsumi Y, Nakagawa S, Ohta T;

DR WPI; 2005-506850/51.
 DR N-PSDB; AEB45441.

XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.

XX Claim 4; SEQ ID NO 11; 34pp; Japanese.

XX The invention relates to tumor necrosis factor (TNF) mutant proteins.
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.

XX SQ Sequence 157 AA;

Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;

QY 1 VRSSRTSPDXPVAVHVNPAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

DB 1 VRSSRTSPDMPVAVHVNPAEQQLWLNRRANALLANGVELRDNLVVPSEGLYLIYS 60

QY 61 QVLFQXGQCPSTHLLTHTTISRIVSYQTPVNLSSAIXSPCQRETPGABAXPWYEPYIL 120

DB 61 QVLFQXGQCPSTHLLTHTTISRIVSYQTPVNLSSAIXSPCQRETPGABAXPWYEPYIL 120

QY 121 GGVFQLEPGDRLSAEINRPDYLDPAESGQVYFGIIAL 157

DB 121 GGVFQLEPGDRLSAEINRPDYLDPFDSNGQVYFGIIAL 157

RESULT 39

AEBA45423

ID AEB45423 standard; protein; 157 AA.

XX AC AEB45423;

XX 22-SEP-2005 (first entry)

XX Human TNF-alpha mutant protein, SEQ ID No:7.

XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoriatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mutein.

XX Homo sapiens.

OS

OS Synthetic.
 XX WO2005066206-A1.
 PN
 XX
 XX 21-JUL-2005.
 PD
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 PF
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 PR
 XX
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
 XX
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45424.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Example 1; SEQ ID NO 7; 34pp; Japanese.
 PS
 XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents human TNF-alpha mutant protein. Note: The sequence data for
 CC this patent did not form part of the printed specification, but was
 CC obtained in electronic format directly from WIPO at
 CC ftp.wipo.int/pub/published_pct_sequences.
 XX
 XX Sequence 157 AA;
 SQ
 Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 0; Mismatches 12; Indels 0; Gaps 0;
 QY 1 VRSSRTSDYVAHVANPQAEQOLWLNRRANALLANGVELRNLQVVPSEGLYLYS 60
 DB 1 VRSSRTSDYVAHVANPQAEQOLWLNRRANALLANGVELRNLQVVPSEGLYLYS 60
 QY 61 QVLFSGQCPSTHVLTTTISRIVSYQTXVNLLSAIXSPCQRETPGEAEXPWYEPYVL 120
 DB 61 QVLFSGQCPSTHVLTTTISRIVSYQTXVNLLSAIXSPCQRETPGEAEXPWYEPYVL 120
 QY 121 GGVFQLEKXGDRLSABINRPDYLDPAESGVYFGIIAL 157
 DB 121 GGVFQLEKXGDRLSABINRPDYLDPAESGVYFGIIAL 157

AC AEB45435;
 XX 22-SEP-2005 (first entry)
 DT
 XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID No:19.
 DE
 XX tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmadium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiarthritic; antiallergic;
 KW antipsoatic; anti-HIV; antiarteriosclerotic; immunosuppressive;
 KW vasotropic; cerebroprotective; dermatological; immunomodulator;
 KW antimalarial; antibacterial; hepatotropic; neuroprotective; nootropic;
 KW mitein.
 XX Homo sapiens.
 OS Synthetic.
 OS
 XX WO2005066206-A1.
 PN
 XX 21-JUL-2005.
 PD
 XX 05-JAN-2005; 2005WO-JP000032.
 PF
 XX 06-JAN-2004; 2004JP-00001427.
 PR
 XX (HAYB) HAYASHIBARA SEIBUTSU KAGAKU.
 PA (MAYU/) MAYUMI T.
 PA (TSUT/) TSUTSUMI Y.
 PA (NAKA/) NAKAGAWA S.
 XX
 XX Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
 XX
 XX WPI; 2005-506850/51.
 DR N-PSDB; AEB45449.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 PT and/or preventing diseases such as inflammation, and other diseases
 PT caused by overexpression of TNF, such as autoimmune diseases, tumor,
 PT rheumatoid arthritis, allergy.
 XX
 XX Claim 4; SEQ ID NO 19; 34pp; Japanese.
 PS The invention relates to tumor necrosis factor (TNF) mutant proteins,
 CC particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 CC TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 CC a TNF mutant protein comprising an amino acid sequence derived from the
 CC human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 CC one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 CC N-terminus, and amino acid residues at positions 84-89 by other amino
 CC acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 CC mutant protein; and (2) a TNF formulation comprising a TNF mutant
 CC protein. The TNF mutant proteins are useful for treating and/or
 CC preventing diseases such as inflammation, and other diseases caused by
 CC overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon
 CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 XX Sequence 157 AA;
 SQ
 Query Match 95.0%; Score 741; DB 1; Length 157;
 Best Local Similarity 92.4%; Pred. No. 0;
 Matches 145; Conservative 1; Mismatches 11; Indels 0; Gaps 0;

RESULT 40
 AEB45435
 ID AEB45435 standard; protein; 157 AA.
 XX

Qy 1 VRSSRTPSDXPAHVAVANPQAEQQLWLNRRANALLANGVELRDNLVVPSSGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVANPQAEQQLWLNRRANALLANGVELRDNLVVPSSGLYLIYS 60
 Qy 61 QVLFQXGQCPSTHVLTHTRISIAVSQTXVNLISATXSPCQRETPEGAEAXPWYEPYIL 120
 Db 61 QVLFQXGQCPSTHVLTHTRISIAVSQTXVNLISATXSPCQRETPEGAEAXPWYEPYIL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIIAL 157
 Db 121 GGVFQLEKXGDRLSAEINRPDYLDPAESGQVYFGIIAL 157

RESULT 41
 AEB45426
 ID AEB45426 standard; protein, 146 AA.
 AC AEB45426;
 XX
 XX
 DT 22-SEP-2005 (first entry)
 XX
 XX TNF-R1 specific human TNF-alpha mutant protein, SEQ ID NO:10.
 XX
 KW tumor necrosis factor-alpha; TNF-alpha; TNF inhibitor; inflammation;
 KW autoimmune disease; tumor; transplant rejection; cardiovascular disease;
 KW acquired immune deficiency syndrome; severe acute respiratory syndrome;
 KW plasmodium infection; meningitis; hepatitis; Alzheimer's disease;
 KW antiinflammatory; cytostatic; antirheumatic; antiallergic; antiallergic;
 KW antiproliferative; anti-HIV; antianticancer; immunosuppressive;
 KW vasotropic; cerebroprotective; hepatotrophic; immunomodulator;
 KW antimalarial; antibacterial; hepatotrophic; neuroprotective; nootropic;
 KW mutein.
 OS Homo sapiens.
 OS Synthetic.
 XX
 XX WO2005066206-A1.
 XX
 XX 21-JUL-2005.
 XX
 XX 05-JAN-2005; 2005WO-JP000032.
 XX
 XX 06-JAN-2004; 2004JP-00001427.
 XX
 XX (HAYB) HAYASHIBARA SEISUTSU KAGAKU.
 XX (MAYU//) MAYUMI T.
 XX (TSUT//) TSUTSUMI Y.
 XX (NAKA//) NAKAGAWA S.
 XX
 XX Mayumi T, Teutsu Y, Nakagawa S, Ohta T;
 XX
 XX MPI; 2005-506850/51.
 XX N-PSDB; AEB45440.
 XX
 XX Novel tumor necrosis factor TNF mutant protein, useful for treating
 XX and/or preventing diseases such as inflammation, and other diseases
 XX caused by overexpression of TNF, such as autoimmune diseases, tumor,
 XX rheumatoid arthritis, allergy.
 XX
 XX Claim 4; SEQ ID NO 10; 34pp; Japanese.

CC cancer, rectal cancer, uterine cancer, brain tumor, leukemia, lymphoma),
 CC Crohn's disease, rheumatoid arthritis, allergies, psoriasis, cachexia,
 CC transplant rejection, stroke, ischemia, restenosis, AIDS, severe acute
 CC respiratory syndrome (SARS), atherosclerosis, Behcet's disease, systemic
 CC lupus erythematosus, malaria, meningitis, hepatitis, Alzheimer's disease,
 CC etc. The TNF mutant proteins are highly stable in vivo. This sequence
 CC represents a human TNF-alpha mutant protein specific for TNF-R1. Note:
 CC The sequence data for this patent did not form part of the printed
 CC specification, but was obtained in electronic format directly from WIPO
 CC at ftp.wipo.int/pub/published_pct_sequences.
 XX
 XX SQ Sequence 146 AA;

Query Match 89.5%; Score 698; DB 1; Length 146;
 Best Local Similarity 93.8%; Pred. No. 0;
 Matches 136; Conservative 1; Mismatches 8; Indels 0; Gaps 0;
 Qy 1 VRSSRTPSDXPAHVAVANPQAEQQLWLNRRANALLANGVELRDNLVVPSSGLYLIYS 60
 Db 1 VRSSRTPSDMPVAHVAVANPQAEQQLWLNRRANALLANGVELRDNLVVPSSGLYLIYS 60
 Qy 61 QVLFQXGQCPSTHVLTHTRISIAVSQTXVNLISATXSPCQRETPEGAEAXPWYEPYIL 120
 Db 61 QVLFQXGQCPSTHVLTHTRISIAVSQTXVNLISATXSPCQRETPEGAEAXPWYEPYIL 120
 Qy 121 GGVFQLEKXGDRLSAEINRPDYLDPA 145
 Db 121 GGVFQLEKXGDRLSAEINRPDYLDPA 145

Search completed: September 21, 2006, 09:09:21
 Job time : 1 secs

XX The invention relates to tumor necrosis factor (TNF) mutant proteins,
 XX particularly tumor necrosis factor mutant proteins specific for TNF-R1 or
 XX TNF-R2 (SEQ ID Nos 19-22 and 37-59 respectively). The invention discloses
 XX a TNF mutant protein comprising an amino acid sequence derived from the
 XX human TNF-alpha protein (given as SEQ ID No: 1) by the substitution of
 XX one or more amino acid residues at 29, 31, 32, 145, 146 and 147 from the
 XX N-terminus, and amino acid residues at positions 84-89 by other amino
 XX acid residue(s). Also described are: (1) a TNF inhibitor comprising a TNF
 XX mutant protein; and (2) a TNF formulation comprising a TNF mutant
 XX protein. The TNF mutant proteins are useful for treating and/or
 XX preventing diseases such as inflammation, and other diseases caused by
 XX overexpression of TNF, such as autoimmune diseases, tumors (e.g. colon